Taiwan Food and Drug Administration

Assessment Report

Trade Name：諾瓦克維德 新型冠狀病毒疫苗 / Nuvaxovid dispersion for injection

Active Ingredient：SARS-CoV-2 rS Omicron XBB1.5

License Number：MOHW-BI 001271

Applicant：頤安國際有限公司

Approval Date：2024/11/05

Indication：
適用於 12 歲以上青少年及成人之主動免疫接種，以預防新型冠狀病毒疾病(COVID-19)。

For active immunization to prevent COVID-19 caused by SARSCoV-2 in individuals 12 years of age and older.

Background Information

Trade Name	諾瓦克維德 新型冠狀病毒疫苗 / Nuvaxovid dispersion for injection
Active Ingredient(s)	SARS-CoV-2 rS Omicron XBB1.5
Applicant	頤安國際有限公司
Dosage Form & Strengths	注射劑 / 5μg per dose
Indication	適用於 12 歲以上青少年及成人之主動免疫接種，以預防新型冠狀病毒疾病 (COVID-19)
Posology	詳如仿單。
Pharmacological Category **ATC Code**	J07BN04

2. Summary Report

2.1 Chemistry, Manufacturing and Controls Evaluation

2.1.1 Drug substance

The SARS-CoV-2 rS protein is the antigen component of a vaccine for use against the evolving SARS-CoV-2. SARS-CoV-2 rS protein is produced by infection of *Spodoptera Frugiperda* (Sf9) insect cells with recombinant baculovirus (BV) engineered to express SARS-CoV-2 rS protein. Purified rS glycoprotein forms trimers that assemble into nanoparticles which bind with high affinity to the human angiotensin-converting enzyme 2 (hACD2) receptor.

The drug substance (DS) manufacturing process begins with the revival and expansion of Sf9 cells, which are infected with baculovirus inoculum (BVI) and incubated until production is complete. Cells are harvested, followed by extraction, low pH treatment, neutralization, clarification and purification to produce a purifiedDS. No animal or human-origin materials are used. Information on the SARS-CoV-2 rS recombinant baculovirus and Sf9 cells is sufficient, and both the virus seed lot system and cell banking system are extensively qualified per ICH guidelines. Process controls and validation confirm the process consistency. Comparability studies, including DS release, extended characterization, and stability, show comparable results from two manufacturing sites.

The structural and functional characteristics of the SARS-CoV-2 rS DS were examined using various orthogonal methods. Sufficient information on impurities has been provided. DS specifications include general tests, protein concentration, identity, purity, potency, residual DNA and safety tests. The validated analytical methods follow ICH guidance. Batch analysis data and CoAs confirm the results are within specifications.

Stability studies on an adequate number of DS batches produced according to the commercial process are ongoing, and available results were provided.

2.1.2 Drug product

The Nuvaxovid (COVID-19) Vaccine is a sterile, preservative-free dispersion for injection containing the SARS-CoV-2 recombinant spike protein, formulated with Matrix-M adjuvant and presented in a 5-dose vial. Matrix-M1, which includes Matrix-A and Matrix-C components, is a novel excipient, and sufficient information has been provided for both. The 1000L batch size is used for commercial production, and all steps, including excipient handling, mixing, and in-process controls have been

validated for process consistency.

The Drug product (DP) specifications include general tests, protein concentration, identity, particle size, potency, Matrix A and C content, safety tests, extractable volume and container closure integrity. Analytical methods are validated per ICH guidance. Batch analysis data and CoAs confirm the results are within specifications. The proposed 12-month shelf-life for DP in the 5-dose vial presentation is supported by long-term stability data from previous Wuhan DP batches. Overall, quality data for Nuvaxovid is sufficient for NDA approval.

2.2 Preclinical Pharmacology/Toxicology Evaluation

2.2.1 Pharmacological Studies

Nuvaxovid with XBB.1.5 strain is composed of the purified recombinant full-length SARS-CoV-2 Omicron XBB.1.5 variant spike protein (rS) in a stabilized prefusion conformation and a saponin-based Matrix-M adjuvant. The design and manufacturing of Nuvaxovid with XBB.1.5 strain are based on the same manufacturing framework as the previously authorized Nuvaxovid prototype COVID-19 vaccine with original, Wuhan, strain, and the non-clinical evaluation of Nuvaxovid with XBB.1.5 strain was limited to immunogenicity studies.

The immunogenicity of the adjuvanted vaccine was evaluated in mouse and non-human primate (NHP) models. Overall, immunization with Matrix-M adjuvanted XBB.1.5 rS monovalent or bivalent vaccines in mice, either as a two-dose primary series or single booster dose, or as a single booster dose in NHPs, induced strong and comparable anti-S IgG, hACE2 blocking Ab and neutralizing Ab titers, as well as T cell responses against several Omicron variants, including XBB.1.5, XBB.1.16, and/or XBB.2.3. The latest data also showed that a two-dose primary series immunization with Matrix-M adjuvanted XBB.1.5 rS monovalent vaccine in monkeys elicited broad cross-reactive anti-S IgG responses and PSVN titers against the variants tested, including Omicron XBB.1.5 and the sublineages. Generally, immunization with XBB.1.5 rS elicited strong responses against the matched antigen, cross-neutralized other XBB sublineages, and reduced antigenic distances between Omicron sublineage variants.

The mice data indicated that the vaccination of monovalent XBB.1.5 rS generally resulted in numerically higher functional antibody titers compared with the other vaccines tested parallelly.

In rhesus macaques, strong anamnestic responses (i.e., immunological memory) were induced following a single booster dose with XBB.1.5 rS 8 months after a primary series vaccination.

Matrix-M adjuvanted SARS-CoV-2 XBB.1.5 rS generally induced Th1-skewed or Th1/Th2 balanced CD4+ T cell responses in mice and NHPs, indicating the risk associated with vaccine-associated enhanced respiratory disease is low.

No challenge-protection studies were planned or performed to investigate the protective efficacy against currently circulating variants of interest (VOIs), i.e., BA.2.86 and JN.1 variants (as of 28 June 2024, WHO), or variants under monitoring

(VUMs) infection conferred by vaccination with SARS-CoV-2 Omicron XBB.1.5 rS adjuvanted with Matrix-M in the animal models.

2.2.2 Toxicological Studies

To support the NDA of SARS-CoV-2 rS variant vaccine(s), 1 pivotal GLP rabbit repeated-dose toxicity study and 1 GLP DART study conducted with SARS-CoV-2 rS and Matrix-M were submitted. All pivotal studies had been submitted previously and reviewed thoroughly to support EUA of Nuvaxovid with Wuhan strain and Nuvaxovid with XBB.1.5 strain vaccines in Taiwan. In a GLP repeated-dose toxicity study in rabbits, IM administration of 50 μg SARS-CoV-2 rS and 50 μg Matrix-M adjuvant (i.e., 10- and 1-fold the proposed human dose, respectively) up to 4 times was well-tolerated and showed no effects except reversible typical responses to active immunization.

2.4 Clinical Efficacy and Safety Evaluation

2.4.1 Efficacy Results

The NDA seeks approval for Nuvaxovid with XBB.1.5 strain, which is intended for active immunization against COVID-19 in individuals aged 12 and older. The applicant submitted several studies across various age groups and variants to support the indication of Nuvaxovid with XBB.1.5 strain. Most of these studies were previously reviewed under the EUA process, primarily involving the original Wuhan strain (NVX-CoV2373) and supported by studies targeting Omicron BA.5 and BA.1 variants. The only new study included in this NDA, which was not part of previous EUAs, is Study 2019nCoV-313 Part 1, focused on evaluating the immunogenicity of a booster dose targeting the XBB.1.5 Omicron subvariant (NVX-CoV2601).

Below is a summary of the studies reviewed in Taiwan's EUA, as well as the new study (Study 2019nCoV-313 Part 1) reviewed in this NDA.

Study 2019nCoV-301 and 2019nCoV-302 (Primary series in adults)

Study 2019nCoV-301 and 2019nCoV-302 are Phase 3, multicenter, randomized, observer-blinded, placebo-controlled trials evaluating the efficacy of NVX-CoV2373 in adults aged 18 and older.

- In Study 2019nCoV-301, NVX-CoV2373 achieved the primary efficacy endpoint compared to placebo, with a vaccine efficacy (VE) of 90.40% (95% CI: [82.88%, 94.62%], 1-sided p-value < 0.001), rejecting the null hypothesis of VE ≤ 30%.
- In Study 2019nCoV-302, the primary efficacy endpoint was also achieved. Interim analysis showed VE at 89.3% (95% CI: [75.2%, 95.4%], 1-sided p-value < 0.0001), while final analysis reported VE at 89.7% (95% CI: [80.2%, 94.6%], 1-sided p-value < 0.001), both rejecting the null hypothesis of VE ≤ 30%.

Study 2019nCoV-301 Pediatric Expansion (Primary series in adolescents)

This pediatric expansion of Study 2019nCoV-301 is a Phase 3, multicenter, randomized, observer-blinded, placebo-controlled trial conducted in adolescents aged 12 to 18. Non-inferiority (NI) of the neutralizing antibody response at Day 35 for adolescent subjects seronegative to anti-SARS-CoV-2 NP antibodies/PCR-negative at baseline compared with that observed in seronegative/PCR-negative adult subjects 18 to < 26 years of age from the adult part of the study was met for all of the 3 pre-specified criteria simultaneously.

- The upper bound of two-sided 95% CI for the ratio of GMTs (GMT18-<26yo/GMT12-<18yo) was < 1.5: GMR 0.7, 95% CI: (0.6, 0.8).

- The point estimate of the ratio of GMTs was ≤ 1.22 (estimated as square root of 1.5): GMR 0.7, 95% CI: (0.6, 0.8).
- The upper bound of the two-sided 95% CI for difference of seroconversion rate (SCR) (SCR18-<26yo – SCR12-<18yo) was < 10%: SCR difference 1.1%, 95% CI: (-0.2%, 2.8%).

Study 2019nCoV-301 Adult Booster Vaccination

A booster dose of NVX-CoV2373 was administered 6 to 14 months after the primary series in adults. Immunogenicity results showed:

- NI was achieved for the ratio of neutralizing antibody GMTs (GMFR), with a LB of the 95% CI > 1.0 (2.7).
- NI was achieved for the difference between post booster and post primary series in neutralizing antibody SCRs, with a LB of the 95% CI > -10% (-7.0%).

Study 2019nCoV-301 Adolescent Booster Vaccination

In the open-label single-dose booster vaccination period of the Pediatric Expansion, a total of 1499 adolescent subjects received a booster dose of NVX-CoV2373. Of these subjects, 220 were randomly selected to Cohort 1 (approximately 110 who received a booster dose after active vaccination during the blinded crossover period) or Cohort 2 (approximately 110 who received a booster dose after active vaccination during the initial [pre-crossover] vaccination period) for the Ad-Hoc Booster PP-IMM Analysis. Only Cohort 2 assessed immunogenicity after both the primary series and booster vaccination periods (Cohort 2 Ad-Hoc Booster PP-IMM Analysis Set).

Results of immunogenicity analyses for Cohort 2 showed.

- NI was achieved for the comparison between the neutralizing antibody (MN50) response against the SARS-CoV-2 wild-type virus (ancestral Wuhan strain) at 28 days after booster administration and that at 14 days after the second dose of NVX-CoV2373 of the primary vaccination series, with a GMFR of 2.7 (95% CI: 2.0, 3.5) and an LB of the 95% CI > 1.0.
- NI of the third (booster) dose of NVX-CoV2373 was achieved for SCR, with an LB of the 95% CI > -10% (the analysis showed a difference of 0.0% [95% CI: -6.8 to 6.8]).

Study 2019nCoV-311 (Part 1 and Part 2)

Study 2019nCoV-311 is a 2-part, Phase 3, randomized, observer-blinded study:

Part 1 evaluated a single booster dose of the Omicron BA.1 subvariant vaccine (NVX-CoV2515) and the prototype Novavax vaccine (NVX-CoV2373) alone and bivalent

prototype and Omicron subvariant vaccines (NVX-CoV2373 + NVX-CoV2515) in previously vaccinated adults 18 to 64 years of age (inclusive) who previously received 2 doses of the Moderna and/or Pfizer-BioNTech prototype vaccines ≥ 180 days prior to study vaccination or 3 doses of the Moderna and/or Pfizer /BioNTech prototype vaccines ≥ 90 days prior to study vaccination.

Results of immunogenicity analyses for Part 1 showed.

- The first primary endpoint was achieved as the Omicron BA.1 subvariant vaccine (NVX-CoV2515) induced a superior response in MN50 GMT versus the prototype Novavax vaccine NVX-CoV2373 against the Omicron BA.1 subvariant virus (130.8 vs 83.9, respectively) using a validated 360biolabs assay at Day 14, with a GMTR of 1.6 (95% CI: 1.33, 2.03) and an LB of the two-sided 95% CI > 1 (1.33).
- The second primary endpoint was achieved as the Omicron BA.1 subvariant vaccine NVX-CoV2515 induced a non-inferior SRR against the Omicron BA.1 subvariant virus versus the prototype Novavax vaccine NVX-CoV2373 (73.4% vs 50.9%, respectively) at Day 14, with a difference in SRRs of 22.5% (95% CI: 10.3, 34.2) and an LB of the two-sided 95% CI > -5% (10.3%).

Part 2 evaluated 2 booster doses of NVX-CoV2540 and the prototype Novavax vaccine (NVX-CoV2373) alone and a bivalent prototype and Omicron subvariant vaccine (NVX-CoV2373 + NVX-CoV2540) in previously vaccinated adults ≥ 18 years of age who had received a regimen of ≥ 3 doses of the Moderna and/or Pfizer-BioNTech monovalent and/or bivalent COVID-19 vaccines ≥ 90 days.

In Part 2, all 3 co-primary endpoints were achieved.

- The first co-primary endpoint demonstrating superiority of the bivalent vaccine (NVX-CoV2373 + NVX-CoV2540) compared to NVX-CoV2373 in regard to the induction of neutralizing antibodies against the Omicron BA.5 subvariant pseudovirus as measured by between-group GMTRs of ID50 GMTs (adjusted) at Day 28
- The second co-primary endpoint demonstrating non-inferiority of the bivalent vaccine (NVX-CoV2373 + NVX-CoV2540) compared to NVX-CoV2373 for the difference in SRRs at Day 28
- The third co-primary endpoint demonstrating non-inferiority of the bivalent vaccine (NVX-CoV2373 + NVX-CoV2540) compared to NVX-CoV2373 in regard to the induction of neutralizing antibodies against the ancestral (Wuhan) strain pseudovirus as measured by between-group GMTRs of ID50 GMTs (adjusted) at Day 28.

Study 2019nCoV-313 Part 1

This study evaluated the safety and immunogenicity of a booster dose targeting the XBB.1.5 Omicron subvariant in adults vaccinated with at least 3 doses of Moderna or Pfizer vaccines.

- The first co-primary endpoint was met, with NVX-CoV2601 showing superior adjusted GMTs against the XBB.1.5 subvariant compared to NVX-CoV2373 (905.9 vs 156.6), with a GMFR of 7.9 (95% CI: 6.8, 9.2).
- The second co-primary endpoint demonstrated non-inferiority in SCRs, with a difference of 57.2% (95% CI: 50.5%, 63.2%) between the NVX-CoV2601 booster (64.3%) and the NVX-CoV2373 booster (7.0%).

Overall, both co-primary endpoints were achieved in Study 2019nCoV-313 Part 1.

2.4.2 Safety Results

The safety profile of Nuvaxovid was based on clinical trials of NVX-CoV2373 (prototype vaccine) and two variant-containing boosters (NVX-CoV2515 and NVX-CoV2601). The core package was Study 2019nCoV-301 (Study 301) including main study, pediatric expansion for adolescents and booster analysis for both adults and adolescents and Study 2019nCoV-302 (Study 302). Study 2019nCoV-311 (Study 311) and Study 2019nCoV-313 (Study 313) were designed to evaluate the booster dose of updated vaccine targeting variant strains.

The adult safety database consisted of interim analysis from Study 301 supporting the initial emergency authorization (main part), a short follow-up of the adult booster dose (original booster analysis and booster addendum), Study 302, and Study 311 supporting the use of updated vaccines. Study 301 was a crossover design for the two-dose primary vaccination. After the vaccine emergently authorized, the testing group and the placebo group would remain blinded and cross over to receive two doses of the other vaccine. This interim analysis did not include data after the blinded cross-over, thus the safety set includes 19,729 participants with a median follow-up time of 98 days for those who received the second dose of NVX-CoV2373, and 9,863 participants with a median follow-up time of 76 days for those who received the second dose of placebo.

The safety set of original booster analysis in Study 301 included selected populations to two cohorts that sequentially receiving two doses of placebo and two doses of NVX-CoV2373 (Cohort 1, n=142), or two doses of NVX-CoV2373 and two doses of placebo (Cohort 2, n=156), in initial vaccination period. The booster addendum provides safety data for all participants (n=12,777) who received booster vaccination. Median duration between the time of the second dose of NVX-CoV2373 and the time of the booster dose was 8.1 months in Cohort 1, 11.2 months in Cohort 2, and 11.0 months in all 12,777 participants. Median follow-up duration of population in booster addendum was 2.0 months after the boost dose. Study 302 had identical design as Study 301. The interim analysis of Study 302 included 7,467 participants with a median follow-up time of 90 days for those who received the second dose of NVX-CoV2373, and 7,463 participants with a median follow-up time of 90 days for those who received the second dose of placebo. Study 311 and Study 313 enrolled adults previously vaccinated 3 or more doses of mRNA vaccine. Median time between last previous COVID-19 vaccine and the booster dose was about 24 to 56 weeks. Median follow-up post booster administration was less than 10 weeks.

- Primary vaccination of NVX-CoV2373

  Solicited local and systemic AEs were recorded by each participant from each dose until 7 days after the vaccination. Following each primary vaccination in all participants of Study 301 main part (2-dose primary vaccination), there was a higher frequency of solicited local and systemic AEs in the NVX-CoV2373 group than in the placebo group. Tenderness and pain were the most frequent solicited local AEs in the NVX-CoV2373. Fatigue, headache, muscle pain, and malaise were the most frequently recorded in the NVXCoV2373 group.

  Besides, the frequency of solicited AEs of NVX-CoV2373 group increased relative to the first vaccination. Majority of participants reported grade 1 or grade 2 events. Participants in the older age cohort (≥ 65 years of age) reported lower frequencies and intensities of solicited AEs among NVX-CoV2373 recipients after each vaccination than in participants in the younger age cohort (18 to ≤ 64 years of age). Grade 4 fever among NVX-CoV2373 recipients was rare, and seldom occurred in the older age cohort. There was a higher incidence of unsolicited AEs reported from start of first vaccination through 28 days after second vaccination in the NVX-CoV2373 group (16.3%) than in the placebo group (14.8%). Incidence that were > 3.00 events/100 patient-year in the NVX-CoV2373 group were headache, fatigue, injection site pain, pyrexia, nasal congestion, myalgia, diarrhea, and nausea. Preferred terms of most TEAEs reported in NVX-CoV2373 recipients appeared to reflect the reactogenicity.

  Unsolicited serious AEs were reported in similar incidence in the NVX-CoV2373 group (4.32 e/100 PY) and placebo (4.89 e/100 PY). In the NVX-CoV2373 group, serious AEs included 1 event of myocarditis. A total of 14 participants died during the study, with 9 in the NVX-CoV2373 group and 5 in the placebo group. All deaths in the NVX-CoV2373 group were assessed as not related to the study vaccine. Similar patterns of response in terms of frequency and intensity were seen in the Study 302. Unsolicited serious AEs were reported in similar frequency in the NVX-CoV2373 group and placebo. In the NVX-CoV2373 group, serious AEs included 1 event of myocarditis. A total of 3 participants died during the study, with 2 in the NVX-CoV2373 group and 1 in the placebo group. All deaths in the NVX-CoV2373 group were assessed as not related to the study vaccine.

- Booster dose of NVX-CoV2373 (the 3rd dose) in adults

Solicited local and systemic AEs within 7 days after the booster dose of NVX-CoV2373 were reported in 83.3% and 82.5%, respectively, of participants in Cohort 1 and 79.8% and 78.2% of participants in Cohort 2, with the majority of events being grade 1 or grade 2 in severity. Solicited events with higher frequency after the booster dose are similar to those events after receiving two doses of the primary vaccination. Frequencies of solicited AEs, any grade and grade ≥ 3 solicited AEs slightly increased with each successful dose (primary series and booster vaccination) of NVX-CoV2373. By data extracted from Booster Addendum (n=10137), solicited local and systemic AEs within 7 days after the booster dose of NVXCoV2373 were reported by 78.9% and 72.0% of participants, respectively, with the majority of events being grade 1 or grade 2 in severity.

Frequencies of unsolicited AEs reported during the 28 days after the booster vaccination were low and comparable across the main study of Study 301 (4.9% for Cohort 1 and 2.6% for Cohort 2 in the original booster analysis and 4.3% for Cohort 1 and Cohort 2 combined in the booster addendum). Among 12,777 participants in the Cohort 1 and Cohort 2 combined in the booster addendum, “Infection and Infestation” was the most frequent (> 1%) SOC and COVID-19 was the most frequent (> 0.5%) AE. A total of 8 deaths were reported after booster vaccination. Events included 3 of cardiac arrest, road traffic accident, esophageal adenocarcinoma stage IV, arrhythmia, sepsis, and septic shock. All 8 deaths were assessed by the investigator and sponsor as not related to study vaccine. Frequencies of SAEs reported after the booster vaccination were also low and comparable across the main study of Study 301 (0% for Cohort 1 and 1.3% for Cohort 2 in the original booster analysis and 0.6% for Cohort 1 and Cohort 2 combined in the booster addendum). The most frequent SAEs (> 3 participants) were COVID-19, acute respiratory failure, pneumonia, and acute myocardial infarction.

- Booster dose of updated vaccine in adults
  The frequency and characteristics of solicited events after receiving a booster dose of NVX-CoV2515 (BA.1), NVX-CoV2540 (BA.5), bivalent vaccines, or NVX-CoV2601 (XBB.1.5) are comparable with vaccine recipients with NVX-CoV2373 (original). Twenty-nine (8.7%) participants reported at least 1 unsolicited AE through 28 days after booster vaccination with NVX-CoV2601. There were no deaths, treatment-related SAEs, AESIs (PIMMC or COVID-19 related), myocarditis/pericarditis after receiving a booster dose of

NVX-CoV2601. None of new risk signal was detected.

The adolescent safety database provided a total of 2,232 adolescent participants received at least 1 dose of NVX-CoV2373 (n=1,487) or placebo (n=745) from the pediatric extension part of Study 301. This analysis also did not include data after the blinded crossover, and the median follow-up time was 71 days for adolescents who received the second dose of NVX-CoV2373. The booster part of pediatric extension had identical design as the original booster analysis in adults. The safety set of booster analysis included Cohort 1 (n=110) and Cohort 2, (n=110) in initial vaccination period, and unrestricted safety set of 1,499 participants which represented not fully cleaned data. The median duration between the time of the second dose of NVX-CoV2373 and the time of the booster dose was 9.0 months (min- max 6-12) in Cohort 1 and 2. The median follow-up duration of population in Cohort 1 and 2 was 52 days after the boost dose.

- Primary vaccination of NVX-CoV2373
  Following each primary vaccination in all participants of Study 301 pediatric extension part (2-dose primary vaccination), there was a higher frequency of solicited local and systemic AEs in the NVX-CoV2373 group than in the placebo group. Injection site tenderness and pain remained the most frequent solicited local AEs while muscle pain, headache, fatigue, and malaise were the most frequent solicited systemic AEs. Majority of adolescent participants reported grade 1 or grade 2 events. Unsolicited AEs with onset from after Dose 1 through the end of the study or administration of crossover vaccination occurred at similar frequencies in the NVX-CoV2373 group and in the placebo group (16.3% and 15.8%, respectively). The most frequent TEAEs (>1.0%) were nasal congestion, headache, cough, and oropharyngeal pain in the NVX-CoV2373 group and upper respiratory tract infection, oropharyngeal pain, nasal congestion, headache, and rhinorrhea in the placebo group. Myocarditis was not observed. This observation is consistent with common diseases in the adolescent background. SAEs were reported in 7 (0.5%) participants in the NVX-CoV2373 group and 2 (0.3%) participants in the placebo group. Only 1 SAE (intentional overdose) was reported in 2 participants (both in the NVX-CoV2373 group). All SAEs were assessed by the investigator as not related to study treatment. There were no deaths among the adolescent participants.

- Booster dose of NVX-CoV2373 (the 3rd dose) in adolescents
  The pre-specified safety analysis was restricted to 220 participants. The safety

profile of the booster dose in adolescents was similar to that in adults. Consistent with adults, the frequency, any grade and grade ≥ 3 solicited AEs of solicited adverse events tend to increase with each dose. Unsolicited AEs through 28 days after the booster dose of NVX-CoV2373 were reported in 11 (5.0%) adolescent participants including 2 (0.9%) participants reporting lymphadenopathy. No TEAE leading to study discontinuation, resulting in death, or AESI (including PIMMCs and COVID-19 related TEAEs). One adolescent participant reported an SAE of cholelithiasis and assessed as unrelated to the vaccination.

2.5 Bridging Study Evaluation

The applicant provided two Japanese studies (TAK-019-1501, TAK-019-3001), safety surveillance report in South Korea and “Novavax Descriptive Pharmacovigilance Comparative Analysis” to support that the ethnic differences of Nuvaxovid is minimal. Based on the available data, no clinically relevant difference in immunogenicity and safety were observed in the East Asian population using Novavax in comparison with non-Asian. Additionally, with over 600,000 doses of the prototype vaccine (Nuvaxovid with Wuhan strain) and 200,000 doses of the variant vaccine administered domestically, no new risk signals have been identified. Therefore, it is recommended that the bridging study be waived.

2.6 Conclusion

Based on the review of data on quality, non-clinical pharmacology/toxicology, safety and efficacy, CDE considers by consensus decision that the benefit-risk balance of Nuvaxovid is favorable in the following indication: Nuvaxovid is indicated for active immunization to prevent COVID-19 in individuals 12 years of age and older.

3. Post-Marketing Requirements

Provide the final version of complete study report after completing study “2019nCoV-314”.

Provide the final version of complete study report after completing study “2019nCoV-313”.