Provisional Consent to the Distribution of a New Medicine

Pursuant to section 23(1) of the Medicines Act 1981, the Minister of Health hereby provisionally consents to the sale, supply or use in New Zealand of the new medicine set out in the Schedule hereto:

Schedule

Product:	**NUVAXOVID**
Active Ingredient:	SARS-CoV-2 rs 10mcg/mL
Dosage Form:	Suspension for injection
New Zealand Sponsor:	Biocelect New Zealand Limited
Manufacturer:	Serum Institute of India Pvt Limited, Pune, India

Provisional consent is granted for a period of nine months.

This consent is given subject to the following conditions.

The New Zealand Sponsor must fulfil the following obligations within the timelines specified, which may be altered by mutual agreement with Medsafe:

1. Prepare a “Dear Healthcare Professional” letter or comparable instructive material and provide this to Medsafe for review and approval prior to distribution of these products. Due date: 18 February 2022.
2. Only batches that have been released for supply by an approved finished product manufacturing or testing site may be supplied in New Zealand.
3. The New Zealand site of batch release will only release batches for distribution in New Zealand once the sponsor has verified that the shipping temperature profile meets specifications.
4. Provide Certificates of Analysis produced by an approved finished product testing site and TGA batch release certification to Medsafe for the first three batches of vaccine intended to be distributed in New Zealand, prior to distribution.
5. Provide independent batch certification, such as UK National Institute for Biological Standards and Control (NIBSC) certification, EU Official Control Authority Batch Release (OCABR) certification, Australian TGA batch release assessment, or any other certification agreed with Medsafe, on request.
6. Provide information to confirm whether report QAG_07905 suitably demonstrates the quantitative capability of the SDS-PAGE drug substance testing method. Due date: 15 February 2022.
7. Provide updated analysis of stability data for drug substance manufactured at SIIPL. Due date: 15 February 2022.
8. Provide the results from testing of drug substance (2,000 L scale) manufactured at SIIPL for Sf-rhabdovirus RNA and endogenous reverse transcriptase, as well as calculation of the residual risk of contamination per finished product dose. Due date: 15 February 2022.
9. Provide data from the thermal stress studies in support of comparability between FDBU and SIIPL drug substance lots. Interim report due date: 15 February 2022. Final report due date: 28 February 2022.
10. Provide the results from the study to demonstrate specificity of the western blot drug substance identity test. Due date: 15 February 2022.
11. Provide an updated analytical comparability report for finished product manufactured at PAR and SIIPL (report QAG_07396), which should contain the 3-month and 6-month thermal stress time points. Updated report due date: 15 February 2022. Final report due date: 31 March 2022.
12. Provide data from a supporting short-term stability study that includes both polypropylene and polycarbonate syringes under various potential extended in-use environmental conditions. Due date: 15 February 2022.
13. Provide a final validation report for the protein assay finished product testing method that includes validation of robustness and sample stability. Due date: 15 February 2022.
14. Provide the full investigation report of the atypical low protein concentration results in the long term finished product stability studies for finished product lots 28003 and 28004 manufactured at PAR. Due date: 15 February 2022.
15. Provide the finalised results from testing of SIIPL Sf9 working cell bank and baculovirus seed viruses. Due date:

15 February 2022.

16. Provide the final report from the leachables study for the PETG bottle used to store adjuvant components. Due date: 15 February 2022.
17. Provide protocols for the full-scale evaluation of chromatography resin lifetimes. Due date: 15 February 2022.
18. Provide the updated drug substance PPQ summary report, including the PPQ host cell protein data. Due date: 15 February 2022.
19. Provide a comparison between mass spectrometry and SDS-PAGE data for both FDBU and SIIPL drug substance lots. Due date: 15 February 2022.
20. Provide extended characterisation data (using techniques described in QAG_07372) for drug substance manufactured using SIIPL working virus seed and working cell bank. Due date: 28 February 2022.
21. Provide monthly updates for the three PPQ drug product lots manufactured at SIIPL using the 50 L manufacturing process and three PPQ drug product lots manufactured at SIIPL using the 2000 L manufacturing process. Due dates: 28 February 2022, 31 March 2022, 30 April 2022, 31 May 2022.
22. Provide a routine stability testing protocol for the Master Cell Bank and Working Cell Bank. Due date: 1 March 2022.
23. Determine the sequence for the Pre-Master Virus Stock, Master Virus Stock, Working Virus Stock, and the virus in the culture harvest collected from the production bioreactor, and provide the report and certificates of analysis. Due date: 1 March 2022.
24. Provide a routine stability testing protocol for the Master Virus Seed and Working Virus Seed. Due date: 1 March 2022.
25. Provide an updated risk assessment that will represent all studies, justifications and technical considerations for the use of Next Generation Sequencing (NGS), and to ensure that it reflects the current control strategy and viral clearance study results. This evaluation should also include comparison of the in vitro pharmacopeial method and the NGS test methods used at Epidote Healthcare. Due date: 31 March 2022.
26. Introduce testing of the baculovirus inoculum and/or the fermenter harvest for mycobacteria in alignment with Ph Eur 2.6.16 requirements for virus harvests, or provide evidence to justify its absence. Due date: 31 March 2022.
27. Validate and implement the improved mass spectrometry method to quantitate the levels of rS and seven predominant host cell proteins in drug substance lots, and set specifications after testing 10 active substance lots. Due date: 31 March 2022.
28. Implement a negative control criterion in the western blot drug substance identity test. Due date: 31 March 2022.
29. Provide the full process validation report for the 2000 L finished product manufacturing process at the SIIPL Manjari premises once the results of the labelled lots (appearance, identity) are in place. Due date: 31 March 2022.
30. Perform a shipping qualification study in order to evaluate the real-world impact of movement, vibration and agitation on the quality of the vaccine. Due date: 31 March 2022.
31. Provide updated specifications for non-compendial raw materials used in the manufacture of drug substance at SIIPL that include an identity test method. Due date: 1 April 2022.
32. Provide results from baculovirus titre testing during manufacture of drug substance at the 2,000 L scale at SIIPL and calculate the residual risk of baculovirus contamination per dose of the finished product. Due date: 30 April 2022.
33. Introduce a relevant suitability requirement to the test used to measure PS80 content in the drug substance. Due date: 30 April 2022.
34. Characterise the glycosylation profile for the next 10 drug substances batches manufactured at SIIPL and provide an evaluation of the need for any further monitoring or control of the glycosylation profile. Due date: 30 June 2022.
35. Develop a host cell protein (HCP) ELISA assay to better control HCP impurities in the drug substance. Once a suitable assay is qualified, it should be implemented to demonstrate in-process HCP clearance. Due date: 30 June 2022.
36. Screen the most abundant host cell protein/host virus proteins present at > 0.5% of total protein for an overlap in

epitopes with human proteins and provide the results. Due date 30 June 2022.

37. Update the procedure for screening for infectious baculovirus to confirm the titre of the positive control and to include a positive control generated by spiking into a test sample. Due date: 30 June 2022.
38. Provide a re-evaluation of the drug substance and finished product total protein specification limits after the statistical analysis of 30 commercial scale lots and implement a shelf-life specification for purity of active substance using SDS-PAGE. Due date: 30 June 2022.
39. Develop an HPSEC-MALS method intended to provide a qualitative assessment of the various structures present in the drug substance. Due date: 30 June 2022.
40. Develop a purity test for finished product using SDS-PAGE and establish a release and shelf-life purity specification. Due date: 30 June 2022.
41. Revise the Matrix-A and Matrix-C specifications and implement the same acceptance limits at release and shelf-life, unless otherwise justified. Due date: 30 June 2022.
42. Provide a justification for the absence of testing PS80 content in the finished product with regards to quality, safety and efficacy across its shelf life, including any possible effects on particulate formation. Due date: 31 July 2022.
43. Provide saponin integrity characterization data for finished product lots collected at release and during stability assessment until there is data for a sufficient number of batches (i.e. n= 30) at commercial scale, covering all sites of antigen and Matrix production. Due date: 31 July 2022.
44. Provide characterisation data for adjuvant ingredients (Matrix-A and Matrix-C) manufactured at full-scale. Due date: 31 July 2022.
45. Provide data to bridge the reference standards used during product development and review the finished product potency limits. Due date: 31 July 2022.
46. Inform Medsafe of any results arising during the ongoing product container leachables study that indicate unsuitability and provide the final study report. Due date: 30 September 2022.
47. Include mean particle size and polydispersity index by dynamic light scattering in the drug substance and finished product release and stability specifications. Due date: 30 September 2022.
48. Develop a CE-SDS method and provide identification of the peaks in the final electropherogram, including a discussion of the data and final confirmation of the molecular weights. Upon completion of successful method development and validation, implement justified acceptance criteria for drug substance and finished product release and stability testing. Due date: 31 December 2022.
49. Provide the final report for non-clinical study NVX 702-115. Due date: 31 March 2022.
50. Provide interim and final reports for non-clinical study NVX 702-087 within five working days of them being produced.
51. Provide the final report for the mouse biodistribution non-clinical study C1810121. Due date: 31 March 2022.
52. Provide further efficacy and safety data from the pivotal clinical studies, including the crossover parts of the studies, within five working days of reports being produced.
53. Provide any reports on the requirement for and timing of booster doses within five working days of these being produced.
54. Provide immunogenicity and safety data regarding use of NUVAXOVID as a booster dose following two doses of the Comirnaty vaccine (from the UK COV-BOOST study) within five working days of reports being produced.
55. Provide Delta strain efficacy information from the adolescents 12–17 years of age expansion component of the US study 2019nCoV-301. Due date: 31 March 2022.
56. Investigate the ability of the vaccine to neutralise emerging SARS-CoV-2 variants and provide associated reports within five workings of these being produced.
57. Provide any reports on efficacy including asymptomatic infection in the vaccinated group, vaccine failure, immunogenicity, efficacy in population subgroups and results from post-marketing studies, within five working days of these being produced.
58. Provide the interim and final reports for clinical studies 2019nCoV-301 and 2019nCoV-302. Interim report due date: 30 June 2022. Final report to be provided within five working days of being produced.

59. Provide the interim and final reports for the ICMR/SII Covovax clinical study. Interim report due date: 28 February 2022. Final report to be provided within five working days of being produced.
60. Provide Periodic Safety Update Reports according to the same schedule as required by the EMA.
61. Provide monthly safety reports, as well as all safety reviews they conduct or become aware of.
62. Perform the required pharmacovigilance activities and interventions detailed in the agreed RMP and any agreed updates to the RMP. An RMP should be submitted at the request of Medsafe or whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important milestone being reached.

Dated this 3rd day of February 2022.

CHRIS JAMES, Group Manager, Medsafe, Ministry of Health (pursuant to delegation given by the Minister of Health on 11 September 2013).

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