NUVAXOVID

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
II/0058/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or	31/10/2023	31/10/2023	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion 'Nuvaxovid-H-C-005808-II-0058-G' * *Pending

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.d - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New manufacturer of material for which an assessment is required of viral safety and/or TSE risk B.I.a.1.d - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New manufacturer of material for which an assessment is required of viral safety and/or TSE risk B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for				

	the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.6.a - Changes to the active substance of a vaccine against human coronavirus - Replacement or addition of a serotype, strain, antigen or coding sequence or combination of serotypes, strains, antigens or coding sequences for a human coronavirus vaccine B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation				

	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method A.7 - Administrative change - Deletion of manufacturing sites B.II.b.3.e - Change in the manufacturing process of the finished or intermediate product - Introduction or increase in the overage that is used for the AS B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data A.6 - Administrative change - Change in ATC Code/ATC Vet Code				

II/0045	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/10/2023	30/10/2023	SmPC and PL	In support of this variation to include a booster recommendation for adolescents for Nuvaxovid, the MAH provided three clinical study reports (and annexes) for study 2019nCOV-301 investigating homologous booster doses for adolescents and adults. The presented dataset shows that the immune response is in line with the immune response previously seen in adults; the submitted adult data is aligned with data already included in the SmPC for homologous booster response. Therefore, since Nuvaxovid has been shown to induce a comparable immune response and effectiveness after the primary series in adolescents as in adults, and because of the ability to boost the vaccine-induced immune response was shown in adults, the CHMP is of the opinion that a booster response to the vaccine is equally expected in adolescents. Besides, the safety profile was shown to be largely similar to the previously observed safety profile for the adolescents and adult booster populations. Based on the above-mentioned extrapolation of immunogenicity of the booster dose in adult and the related safety profile, the CHMP agrees with the inclusion of a booster dose recommendation for the adolescent population in the section 4.2 of the SmPC. Sections 4.8 and 5.1. are updated accordingly, with the dataset from studies evaluating a booster dose in both adolescents and adults' populations. For more information, please refer to the Summary of Product Characteristics.
IB/0057/G	This was an application for a group of variations. B.III.2.b - Change to comply with Ph. Eur. or with a	15/09/2023	n/a		

	national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.I.z - Quality change - Active substance - Other variation B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.2.e - Change in test procedure for AS or				

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
II/0054	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	31/08/2023	n/a		
IB/0056/G	This was an application for a group of variations. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished	30/08/2023	n/a		

	product - Tightening of in-process limits B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits				
IB/0055/G	This was an application for a group of variations. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	07/08/2023	n/a		
PSUSA/10972 /202212	Periodic Safety Update EU Single assessment - SARS-CoV-2, spike protein, recombinant, expressed in sf9 cells derived from spodoptera frugiperda (Nuvaxovid)	06/07/2023	n/a		PRAC Recommendation - maintenance
II/0048/G	This was an application for a group of variations.	25/05/2023	04/07/2023	SmPC and	The SmPC section 6.3 has been updated to reflect the

	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range			Annex II	extended shelf life of the unopened vial: 12 months at 2°C to 8°C, protected from light. The SmPC section 5.1 has been updated by deleting the text below: "This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited. The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary." The PL have been updated accordingly. The following two specific obligations are deleted from the Annex II to the Opinion: In order to ensure consistent product quality during shelf life, the MAH should provide additional information on stability of the finished product. In order to ensure consistent quality over the product life cycle, the MAH should adequately bridge the reference standards and review the finished product potency limits when additional data become available. In light of all available data, the benefit-risk balance of NUVAXOVID remains positive and considering fulfilment of all specific obligations, the Conditional Marketing Authorisation of Nuvaxovid can be converted to a Marketing Authorisation not subject to specific obligations.
IB/0053/G	This was an application for a group of variations. B.II.e.5.a.2 - Change in pack size of the finished	22/06/2023	30/10/2023	SmPC, Labelling and	

	product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes			PL	
IB/0051/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.a - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits for medicinal products subject to OCABR	25/05/2023	n/a		
IAIN/0052	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/05/2023	n/a		
IB/0050	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	16/05/2023	n/a		
IB/0049/G	This was an application for a group of variations.	21/04/2023	n/a		

	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation				
IB/0043	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	20/04/2023	n/a		
IA/0047	B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	12/04/2023	n/a		
IB/0046/G	This was an application for a group of variations. B.II.b.z - Change in manufacture of the Finished Product - Other variation B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	12/04/2023	n/a		
IB/0042/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.b.2.a - Change in test procedure for AS or	01/03/2023	n/a		

	starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0039/G	This was an application for a group of variations. B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.5.c - Change in pack size of the finished product - Change in the fill weight/fill volume of sterile multidose (or single-dose, partial use) parenteral medicinal products, including biological/immunological medicinal products B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	23/02/2023	04/04/2023	SmPC, Labelling and PL	The SmPC sections 2, 6.5, 6.6 and 8 have been updated to reflect the new 5-dose vial presentation. In addition, changes have been included to align with the latest QRD template and SmPC guidance. The Labelling and package leaflet have been updated accordingly.
II/0035/G	This was an application for a group of variations. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS B.I.a.1.j - Change in the manufacturer of AS or of a	16/02/2023	04/04/2023	Annex II	

	starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
PSUSA/10972 /202206	Periodic Safety Update EU Single assessment - SARS-CoV-2, spike protein, recombinant, expressed in sf9 cells derived from spodoptera frugiperda (Nuvaxovid)	12/01/2023	n/a		PRAC Recommendation - maintenance
IB/0037/G	This was an application for a group of variations. B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol	06/01/2023	n/a		
IB/0041	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	04/01/2023	n/a		
IB/0040/G	This was an application for a group of variations. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	22/12/2022	n/a		

	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data				
IB/0036/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	15/12/2022	n/a		
II/0034	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method	15/12/2022	n/a		
IB/0033	B.II.f.1.b.2 - Stability of FP - Extension of the shelf	15/12/2022	05/01/2023	SmPC,	To extend the punctured vial shelf life from 6 hour at 2°C

	life of the finished product - After first opening (supported by real time data)			Labelling and PL	to 25°C to 12 hours at 2°C to 8°C or 6 hours at room temperature (maximum 25°C) from the time of first needle puncture to administration.
II/0027	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	08/12/2022	n/a		
IB/0038	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	02/12/2022	n/a		
II/0028	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	01/12/2022	n/a		
IB/0032	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	17/11/2022	n/a		
IB/0031	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	20/10/2022	n/a		

II/0025/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	20/10/2022	n/a		

IB/0029	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	14/10/2022	n/a		
II/0011/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	13/10/2022	n/a		
R/0020	Renewal of the marketing authorisation.	15/09/2022	03/10/2022		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for NUVAXOVID, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. Please refer to Scientific Discussion 'Nuvaxovid/H/C/005808/R/0020'.
II/0022	Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on pericarditis and myocarditis and to add pericarditis and myocarditis to the list of adverse drug reactions (ADRs) with frequency 'Not known' following the outcome of MEA 014.4 based on PRAC assessment on pericarditis and myocarditis. The Package Leaflet is updated accordingly. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure	29/09/2022	05/01/2023	SmPC and PL	There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) following vaccination with Nuvaxovid. These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general. Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees

	concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH				(including parents or caregivers) should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. For more information, please refer to the Summary of Product Characteristics.
IB/0023/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	14/09/2022	n/a		
IA/0026	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	13/09/2022	n/a		
II/0014	Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include a third dose for Nuvaxovid, to boost individuals who have previously completed a primary vaccination series with Nuvaxovid (homologous booster dose) or with an mRNA or adenoviral vector vaccine (heterologous booster dose); based on interim data from study 2019nCoV-101 (Part 2), final data from study 2019nCoV-501, and data from the COV-BOOST study; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been	01/09/2022	06/09/2022	SmPC and PL	The homologous third booster recommendation is supported by data from studies 2019nCoV-101 (Part 2) and 2019nCoV-501; both are randomised, placebo-controlled, observer-blinded clinical trials. The results from study 2019nCoV-101 (part 2) indicated an approx. 86.7-folder increase of neutralising antibody geometric mean titres (GMTs) post-boost compared to pre-boost, 28 days following booster vaccination. The observed titres were approx. 4.1-fold greater than titres reported following the primary vaccination series. A similar response was not

	approved. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				observed in the placebo group. The results from study 2019nCoV-501 showed that 35 days after the booster dose the neutralising antibody GMT were 2-fold higher than those measured 7 days after the primary vaccination series as given to the placebo-arm. Also, titres at post-booster dose)were higher than at post-primary series in subjects initially randomised to the Nuvaxovid group. This is suggestive of an adequate boosting response. Moreover, the results from 2019nCoV-501 indicated a consistent response in people living with HIV, albeit of a lower magnitude. The reactogenicity with the third booster dose given 6 months following the second dose was acceptable. With the third dose an increase in the frequency and severity of local and systemic reactions was observed as compared to the second dose although they were transient (median duration of 1 to 3 days following vaccination). The most frequent solicited adverse reactions were injection site tenderness, fatigue, injection site pain, muscle pain, malaise and headache, joint pain, and fever. No new safety concerns were identified. The heterologous booster dose recommendation is supported by data from the COV-BOOST study*. This was a randomised, controlled clinical trial where participants who had received two doses of either an mRNA-vaccine or an adenoviral vector vaccine and had no history of laboratory confirmed SARS-CoV-2 infection were randomised to receive a booster with different a COVID-19 vaccine, including Nuvaxovid as a full dose (as approved in the SmPC) and half dose. In participants who received either a full or half dose, it was observed a 2.6-6.3 fold-increase of neutralising antibody titres 28 days after the booster vaccination compared to the control group (who received a

					single dose of an MenACWY vaccine). This is suggestive of an adequate boosting response. Overall the frequency and severity of local and systemic reactions were similar between the groups that received either full or half dose of Nuvaxovid and control vaccine. No new safety concerns were identified. * Munro et al, 2021 "Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial", Lancet 2021; 398: 2258–76, https://doi.org/10.1016/S0140-6736(21)02717-3.
IB/0021	C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	26/08/2022	06/09/2022	SmPC and PL	SmPC updated in section 4.4 and section 4.8. (Adverse Effects; frequency not known) and also relevant section of package leaflet regarding anaphylaxis, paraesthesia and hypoesthesia following PRAC outcome for MSSR MEA 14.3
IB/0015	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	05/07/2022	n/a		
IB/0013/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.I.b.1.z - Change in the specification parameters	04/07/2022	06/09/2022	Annex II	Addition of SK Bioscience Co. Ltd as a new manufacturing site for the active substance

	and/or limits of an AS, starting material/intermediate/reagent - Other variation				
II/0009	Extension of indication to include use in adolescents 12 to 17 years of age for Nuvaxovid, based on data from study 2019nCoV-301, a Phase 3, Randomized, Observer-Blinded, Placebo-Controlled Study to evaluate the efficacy, safety, and immunogenicity of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) with Matrix-M Adjuvant in Adult Participants ≥ 18 Years with a Pediatric Expansion in Adolescents (12 to < 18 Years); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	23/06/2022	01/07/2022	SmPC and PL	Please refer to Scientific Discussion 'EMEA/H/C/005808/II/0009'
IB/0018	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/06/2022	n/a		
IB/0017/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of	21/06/2022	n/a		

	the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IB/0016	B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation	15/06/2022	n/a		
IB/0012/G	This was an application for a group of variations. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation B.II.c.4.z - Change in synthesis or recovery of a non-	13/05/2022	n/a		

	pharmacopoeial or novel excipient - Other variation				
IB/0010	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	03/05/2022	n/a		
II/0007	B.II.b.3.e - Change in the manufacturing process of the finished or intermediate product - Introduction or increase in the overage that is used for the AS	22/04/2022	n/a		
IB/0008	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	06/04/2022	n/a		
IB/0006/G	This was an application for a group of variations. B.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile) B.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile)	06/04/2022	n/a		
II/0004	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	24/03/2022	n/a		
IB/0005	C.I.z - Changes (Safety/Efficacy) of Human and	18/03/2022	01/07/2022	SmPC,	Sections 4.4, 4.8, 5.3 and 6.4 of the SmPC, section 3 of the

	Veterinary Medicinal Products - Other variation			Labelling and PL	Labelling and sections 2 and 6 of the PL have been updated to include minor corrections.
IB/0003	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	11/03/2022	n/a		
IB/0002/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	02/03/2022	n/a		
IAIN/0001	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	27/01/2022	n/a		