Appendix 14: Search Strategy/Methodology for Safety Topics for Monitoring

Refer to Table 41 for MedDRA search strategy/methodology for safety topics for monitoring.

Table 41: MedDRA Search Strategy/Methodology for Safety Topics for Monitoring

Safety Topic	Section No.	MedDRA[a] Search Strategy/Methodology
Vaccination Errors	9.2	SMQ (broad): Medication Errors
Fatal Reports	15.2.2.1	Seriousness criteria: Death OR Event Outcome = Fatal
Age group: Paediatrics	15.2.2.2.1	Review of safety concerns in individuals < 18
Age group: Elderly	15.2.2.2.2	Review of safety concerns elderly individuals ≥ 65 years
Vaccine Anxiety-Related Reactions	15.2.2.3	HLT: Anxiety symptoms
Cholecystitis	15.2.2.4	HLT: Cholecystitis and cholelithiasis; SMQ: Functional, Inflammatory and Gallstone Related Biliary Disorders
Inflammatory Eye Disorders	15.2.2.5	Customised MedDRA Query (CMQ): HLGT: Ocular infections, irritations, and inflammations + PT: Diplopia; Diplopia correction; Eye swelling; Heteronymous diplopia; Homonymous diplopia; Lacrimation disorder; Lacrimal disorder; Lacrimation increased; Photophobia)
Menstrual Disorders	15.2.2.6	HLGT: Menstrual cycle and uterine bleeding disorders
Paraesthesia	15.1.3	HLT: Paraesthesias and dysaesthesias
Reactogenicity Profile-Second Dose and Boosters (based on impurity levels)	15.2.2.7	HLGT: Administration site reactions; Body temperature conditions; Gastrointestinal motility and defaecation condition; Gastrointestinal sign and symptoms; Headaches; Muscle Disorders. HLT: Asthenic conditions; Feelings and sensations. Filter for patients treated with Dose 2 or booster and with lot information available.
Vaccination Failures/Lack of Efficacy	16.3.5	SMQ (broad): Lack of efficacy/effect
Use in Pregnancy and While Breastfeeding	16.3.6.1	Patient pregnancy = Yes SMQ (broad): Lactation related topics (incl neonatal exposure through breast milk)
Use in Immunocompromised Patients	16.3.6.2	Patient Medical History belonging to: High Level Group Term (HLGT): Immunodeficiency syndromes HLT: Chemotherapies All PTs containing the word ‘transplant’ except for: ‘hair transplant’, ‘corneal transplant’ and ‘thyroid autotransplantation’ PTs: Monoclonal antibody chemoimmunoconjugate therapy; Splenectomy

Table 41: MedDRA Search Strategy/Methodology for Safety Topics for Monitoring

Safety Topic	Section No.	MedDRA[a] Search Strategy/Methodology
Use in Frail patients with comorbidities (e.g., COPD, diabetes, chronic neurological disease, cardiovascular disorders)	16.3.6.3	Patient Medical History belongs to SMQs (broad): Hyperglycaemia/new onset diabetes mellitus; Hypoglycaemia; Immune-mediated/autoimmune disorders; Acute central respiratory depression; Asthma/bronchospasm; Eosinophilic pneumonia; Infective pneumonia; Pulmonary hypertension; Respiratory failure; Embolic and thrombotic events; Cardiac arrhythmias; Cardiac failure; Cardiomyopathy; Ischaemic heart disease; Torsade de pointes/QT prolongation; Acute renal failure; Chronic kidney disease; Renovascular disorders; Hepatic disorders; Biliary disorders; Central nervous system vascular disorders; Convulsions; Dementia; Demyelination; Extrapyramidal syndrome; Peripheral neuropathy
Use in Patients with Autoimmune or Inflammatory Disorders	16.3.6.4	Patient Medical History belonging to SMQ (broad): Immune-mediated/autoimmune disorders
Interaction with Other Vaccines	16.3.6.5	PTs: Drug interaction; Inhibitory drug interaction; Potentiating drug interaction; Labelled drug-drug interaction medication error

[a]MedDRA 25.0

Appendix 15: Australia Regional Appendix

This section presents the additional safety topics and requirements for Australia that are not already discussed in the PBRER.

- Number of Reports in Australia and Global

During the reporting interval and cumulatively, there were 777 spontaneous ICSRs from Australia and 1874 spontaneous ICSRs reported globally.

- Safety Topics for Monitoring for Australia

Monitoring of additional events was performed as per the Australian Public Assessment Report for SARS-CoV-2 rS with Matrix-M adjuvant. During the reporting interval and cumulatively, all ICSRs in the global vaccine safety database were queried for the following safety topics referenced below (refer to Table 42). The topics of myocarditis and pericarditis, thrombocytopenia (refer to Appendix 13 for their search strategy), medication errors and vaccination failures (refer to Appendix 14 for their search strategy) were not included below as these are discussed in Section 15.1.2, Section 15.2.1.16, Section 9.2, and Section 16.3.5 respectively.

Table 42: Safety Topics and MedDRA Search Strategy for Australia

Safety Topic	MedDRA[a] Search Strategy
Angioedema	SMQ (broad): Angioedema
Central retinal vein thrombosis	HLT: Retinal embolism and thrombosis
Colitis	HLT: Colitis (excl. infective)
Hypersensitivity	SMQ (broad): Hypersensitivity
Hypertension	SMQ (broad): Hypertension
Potential Immune-Mediated Medical Conditions (PIMMC)	SMQ (broad); Immune-mediated \autoimmune disorders
Potential interaction concomitant treatments	PTs: Drug interaction; Inhibitory drug interaction; Potentiating drug interaction; Labelled drug-drug interaction medication error
Safety effects of mixed schedules	PTs: Extra dose administered; Inappropriate schedule of product administration; Inappropriate schedule of product discontinuation; Incomplete course of vaccination; Incorrect product administration duration; Incorrect product formulation administered; Interchange of vaccine products; Off-label use; Product administration interrupted; Product dose omission in error; Product dose omission issue; Product substitution; Product substitution error; Product substitution issue; Routine immunisation schedule incomplete; Routine immunisation schedule not administered; Unknown schedule of product administration; Unknown vaccine product administered; Wrong schedule

[a]: MedDRA 25.0

- Summary of Designated Medical Events (DMEs)

DMEs are under surveillance to monitor any trends or changes in frequency of these events.

The global vaccine safety database was queried for interval and cumulative ICSRs with DMEs.

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 23 ICSRs of DMEs which contained 24 AEs including 9 serious, medically confirmed AEs; and 15 serious, non-medically confirmed AEs.

There were 24 serious AEs, most of which were coded to PTs Anaphylactic reaction (n=15), and Angioedema (n=4). Of the 23 ICSRs, 19 were for females and 4 for males; the age range was 25-60 years. The TTO ranged from 0-25 days when reported (n=17), majority being within 0-10 days (n=15,65%). The majority of AEs were serious, non-medically confirmed (n=15, 62.5%). The outcome of most events was reported as recovered at the time of reporting. No significant medical history or concomitant medications were reported for the majority of ICSRs.

The rr was 2.22 per 100,000 doses administered, equivalent to 0.00222% of all doses administered.

- Conclusion

Amongst these DMEs, anaphylactic reaction (under the AESI of anaphylaxis) has been identified as a confirmed signal and further details are presented in Section 15.1.1. A review of other reports did not identify any trends. No safety signal was identified.

- Angioedema

Angioedema is a safety topic under surveillance due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the broad search strategy; SMQ (broad) Angioedema.

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 147 ICSRs of angioedema which contained 175 AEs including 3 serious and 8 non-serious, medically confirmed AEs; and 19 serious and 145 non-serious, non-medically confirmed AEs.

Of the total 175 AEs reported, the most frequently reported PTs included Peripheral swelling (n=34), Urticaria (n=34), Hypersensitivity (n=18), Swelling face (n=14), Swelling (n=12), Throat tightness (n=10) and Eye swelling (n=9). There were 3 serious medically confirmed

reports including angioedema (n=1), hypersensitivity (n=1), and lip oedema (n=1) of which 2 AEs (hypersensitivity, and lip oedema) involved hospitalisation. The majority of AEs were non-serious and not medically confirmed (n=145, 82.85%). The outcome of the majority of events was reported as not recovered at the time of reporting. Of the 147 ICSRs, 119 were for females and 28 for males; the age range was 19-83 years. The TTO ranged from 0-36 days when reported (n=88). No significant medical history or concomitant medications were reported for the majority of ICSRs.

The rr was 14.2 per 100,000 doses administered, equivalent to 0.01422% of all doses administered.

- Conclusion

A review of these reports did not reveal a causal association due to insufficient information. No safety signal was identified.

- Central retinal vein thrombosis

Central retinal vein thrombosis is a safety topic under surveillance due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the specific HLT: Retinal embolism and thrombosis.

During the reporting interval and cumulatively, no ICSRs were retrieved.

- Colitis

Colitis is a safety topic under surveillance for Australia due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the specific HLT: Colitis (excl. infective).

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 4 ICSRs of colitis which contained 4 serious AEs coded to PT Crohn’s disease (n=4) including 1 medically confirmed and 3 non-medically confirmed AEs. The outcome of all the events was reported as not recovered at the time of reporting. All reports concerned females and their ages ranged from 30-39 years. The TTO ranged from 0-15 days when reported (n=3). One report had medical history of nickel allergy and Crohn’s disease. No other significant details were provided.

The rr was 0.39 per 100,000 doses administered, equivalent to 0.00039% of all doses administered.

- Conclusion

A review of these reports did not reveal a causal association due to insufficient information. No safety signal was identified.

- Hypersensitivity

Hypersensitivity is a safety topic under surveillance due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the broad search strategy; SMQ (broad): Hypersensitivity.

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 332 ICSRs of hypersensitivity which contained 446 AEs including18 serious and 17 non-serious, medically confirmed AEs; and 44 serious and 367 non-serious, non-medically confirmed AEs.

Of the total 446 AEs reported, the most frequently reported PTs included Rash (n=122), Pruritis (n=70), Urticaria (n=34), Erythema (n=29), Rash pruritic (n=19), Hypersensitivity (n=18), and Anaphylactic reaction (n=15). The majority of AEs were non-medically confirmed and non-serious (n=366, 82.4%). The outcome of majority of events was reported as not recovered at the time of reporting. Of the 332 ICSRs, 272 were for females and 57 for males; the age range was 19-83 years. The TTO ranged from 0-63 days when reported (n=202). There’s no significant medical history or concomitant medications reported.

The rr was 32.10 per 100,000 doses administered, equivalent to 0.03210% of all doses administered.

- Conclusion

. A review of these reports did not reveal a causal association between the events due to insufficient information.

- Hypertension

Hypertension is a safety topic under surveillance due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the broad search strategy; SMQ (broad): Hypertension.

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 70 ICSRs of hypertension which contained 74 AEs including 7 serious and 4 non-serious, medically confirmed AEs; and 17 serious and 46 non-serious, non-medically confirmed AEs.

Of the total 74 AEs, the most frequently reported PTs included Hypertension (n=40) and Blood pressure increased (n=22). The majority of AEs were non-medically confirmed and non-serious (46, 62%). The outcome of majority of events was reported as not recovered at the time of reporting.

There were 20 ICSRs (28%) that were serious, of which 9 ICSRs (13%) were serious due to a criterion of hospitalisation and contained 10 AEs. These 9 ICSRs are summarised in Table 43. Only two reports had concomitant medications of cetirizine, tamoxifen and metoprolol. Three reports had medical history of hypertension, migraine, tension, headache, pain, drug hypersensitivity, seasonal allergy, lipoedema, ill-defined disorder, and fibromyalgia. The TTO was within 1 hour to 4 days after vaccination in 8 out of 9 hospitalised individuals. The most frequently associated PTs were Headache, Fatigue, and Pain. Limited case details are available for reports overall, including reports involving hospitalisation. ICSRs with co-reported terms related to other safety topics or AESI, including arrhythmias, myocarditis and pericarditis are also reviewed under these topics.

Of the 70 ICSRs reported, 49 were for females and 21 for males; the age range was 28-80 years. The TTO ranged from 0-26 days when reported (n=50).

The rr was 6.77 per 100,000 doses administered, equivalent to 0.00677% of all doses administered.

Table 43: Hypertension Case Series – Serious Due to Hospitalisation

Case Number	Country of Incidence	Patient Age	Patient Sex	Preferred Term/s with Reported Verbatim	Seriousness	Case Summary
4.1(b)	4.1(b)	46 Years	Female	Dyspnoea exertional (Significant exertional dyspnea); Dizziness (Dizziness); Performance status decreased (Massive performance degradation); Lung consolidation (Consolidation of both lungs with reduced ventilation); Post-acute COVID-19 syndrome (Hypertension); Tachycardia (Tachycardia); Hypertension (Hypertension); Headache (Headache); Myalgia (Muscle ache); Fatigue (Exhaustion); COVID-19 immunisation (Revaccination with different covid-19 vaccine); Fatigue (Tiredness)	Hospitalisation	A 46-year-old female was vaccinated with primary dose 1. Medical history was reported as Comirnaty (tozinameran) and "grass, birch, shrimps." No concomitant medications were reported. Four days after vaccination, the individual experienced headache, significant exertional dyspnoea, dizziness, exhaustion, revaccination with different covid-19 vaccine, hypertension, performance status decreased, tiredness, Post-acute COVID-19 syndrome, consolidation of both lungs with reduced ventilation, hypertension, tachycardia, and muscle ache. The report indicated that there was "cardiology, lungs, COVID outpatient clinic, immunological outpatient clinic, treatment with beta blockers, strict physical rest until further notice, and that side effects continue, independently leaving the apartment is not possible. At the time of reporting, the event outcomes of Headache, Dyspnoea exertional, Dizziness, and Fatigue were not recovered/not resolved, COVID-19 immunisation was unknown, Myalgia, Performance status decreased, Fatigue, Lung consolidation, Post-acute COVID-19 syndrome, Tachycardia, and Hypertension were not recovered/not resolved.
4.1(b)	4.1(b)	45 Years	Female	Pericarditis (Pericarditis); Pneumonia (Pneumonia); Burning sensation (Burning sensation); Chest pain (Chest pain); Dyspnoea (Dyspnoea); Paraesthesia (Paraesthesia); Tachycardia (Tachycardia); Confusional state (Confusional state); Dizziness (Dizziness); Electric shock sensation (Electric shock sensation);	Hospitalisation	A 45-year-old fit and healthy female from 4.1(b) with no medical history and concomitant medications experienced medically significant events of Pericarditis, Pneumonia, Confusional state and Dizziness, and was hospitalised due to the aforementioned events and with the following events of Burning sensation, Chest pain, Dyspnoea, Electric shock sensation, Hypertension, Lethargy, Nausea, Pain in extremity, Paraesthesia, Pollakiuria and Tachycardia approximately 13 days after receiving NVX-CoV2373 10 ug/mL (unspecified dose, first dose). Diagnostic

Case Number	Country of Incidence	Patient Age	Patient Sex	Preferred Term/s with Reported Verbatim	Seriousness	Case Summary
				Lethargy (Lethargy); Pollakiuria (Pollakiuria); Echocardiogram abnormal (Echocardiogram abnormal); Tremor (Tremor); Hypertension (Hypertension); Pain in extremity (Pain in extremity); Nausea (Nausea)		tests included Echocardiogram and CT scan of heart (slight inflammation of pericardium and lung infection), Troponin and blood tests (both "good"); the result of the chest x-ray was not reported. The treatment included Amoxycillin and colchicine. The outcome of the events is unknown.
4.1(b)	4.1(b)	47 Years	Female	Myopericarditis (Perimyocarditis); Sleep disorder (Sleep disturbance); Tachycardia (Tachycardia); Hypertension (Hypertension); Headache (Headache); Vomiting (Vomiting); Fatigue (Exhaustion); Nausea (Nausea); Fatigue (Tiredness)	Hospitalisation	A 47-year-old female was vaccinated with intramuscular Nuvaxovid. Eight hours after administration of the vaccine she experienced very severe headache, nausea, vomiting, and high blood pressure. Twenty-hours post vaccination she was transported by ambulance to the hospital, and she receive a diagnosis of hypertension and perimyocarditis 5 days after vaccination. All events were recovered with sequelae.
4.1(b)	4.1(b)	Adult	Male	Heart rate increased (Pulse increased); Blood pressure increased (Pressure blood increased); Dizziness (Light headedness); Chills (Chills)	Hospitalisation	A male of an unspecified age received an unspecified dose of NUVAXOVID. Medical history and concomitant medications were not reported. One day after vaccination, the individual experienced pulse increased, light-headedness, blood pressure increased and chills. He was hospitalised. At the time of reporting, the event outcome of Heart rate increased was not recovered/not resolved, Chills was not recovered/not resolved, Blood pressure increased was not recovered/not resolved and Dizziness was not recovered/not resolved.
4.1(b)	4.1(b)	33 Years	Female	Blood pressure increased (Blood pressure increased); Arrhythmia (Arrhythmia); Dizziness (Light headedness); Visual impairment (Visual disturbance); Headache	Hospitalisation	A 33-year old female was vaccinated with Nuvaxovid. Two days after vaccination, the individual experienced blood pressure increased (168/122 mm of HG), headache, arrhythmia, nausea, tiredness, visual disturbance, and light headedness, and was hospitalized. The following day the blood pressure returned to normal range, light headedness and mild

Case Number	Country of Incidence	Patient Age	Patient Sex	Preferred Term/s with Reported Verbatim	Seriousness	Case Summary
				(Headache); Fatigue (Tiredness); Nausea (Nausea)		nausea. At the time of reporting, the event outcomes of Blood pressure increased, Headache, Arrhythmia, Dizziness, Fatigue, Visual impairment, and Nausea were recovering/resolving.
4.1(b)	4.1(b)	52 Years	Female	Aphasia (Word finding difficulty); Bradyphrenia (Slowed thinking); Feeling abnormal (Foggy feeling in head); Influenza (Flu symptoms); Asthenia (Weakness); Exercise tolerance decreased (Decreased exercise endurance); Migraine (Migraine aggravated); Hypertensive crisis (Crisis hypertensive); Blood pressure fluctuation (Blood pressure fluctuation); Chills (Chills); Fatigue (Prostration); Injection site swelling (Injection site swelling); Myalgia (Myalgia); Injection site pain (Injection site pain); Headache (Persistent headache)	Hospitalisation	A 52-year old female was vaccinated with dose 1 on an unspecified date and dose 2 on 24-Mar-2022. Concomitant medications included metoprolol and medical history included hypertension (since 2008), migraine (since 2005), tension headache (since 2005), permanent headache on the right (since 2015 to mid-2019), and sulfanilamide allergy. One day after vaccination, she experienced prostration, word finding difficulty, slowed thinking, foggy feeling in head, injection site swelling, chills, flu symptoms, weakness, myalgia, injection site pain, and decreased exercise endurance. Two days after vaccination she experienced persistent headache and migraine aggravated. Four days after vaccination she experienced hypertensive crisis and blood pressure fluctuation.
4.1(b)	4.1(b)	32 Years	Female	Paraesthesia (Tingling); Paraesthesia (Paraesthesia); Tachycardia (Tachycardia); Hypoaesthesia (Numbness); Blood pressure increased (Blood pressure increased); Pain in extremity (Pain in arm)	Hospitalisation	A 32-year-old female with history of fibromyalgia, ill-defined disorder, lipoedema, "CVI" and seasonal allergy (hay fever), received NUVAXOVID. Twenty-one days after vaccination, the individual experienced pain in arm, tingling, blood pressure increased (183/100), tachycardia, numbness, paraesthesia. She was hospitalised in cardiologic neurologic departments. At the time of reporting, the outcome of the events was not recovered/not resolved

Case Number	Country of Incidence	Patient Age	Patient Sex	Preferred Term/s with Reported Verbatim	Seriousness	Case Summary
4.1(b) [redacted]	4.1(b)	40 Years	Female	Tremor (Tremor); Somnolence (Sleepiness); Heart rate increased (Heart rate increased); COVID-19 immunisation (Revaccination with different covid-19 vaccine); Lip oedema (Lip oedema); Feeling abnormal (Feeling abnormal); Loss of consciousness (Loss of consciousness); Dyspnoea (Dyspnoea); Oropharyngeal discomfort (pharynx discomfort); Ventricular extrasystoles (Ventricular extra systoles); Muscular weakness (Lower extremities weakness of); White blood cell count increased (Leukocyte count increased); Toothache (Toothache); Blood pressure increased (Blood pressure increased); Vaccination site mass (Vaccination site lump); Sinus tachycardia (Sinus tachycardia); Erythema (Erythema facial); Malaise (Malaise); Fatigue (Fatigue); Vaccination site pain (Vaccination site pain); Hypersensitivity (Allergic reaction NOS)	Hospitalisation	A 40-year-old female was vaccinated with Dose 3 of intramuscular Nuvaxovid. Concomitant medication was reported as tamoxifen citrate and cetirizine. On the same day of vaccination, she experienced tremor, Somnolence, Heart rate increased, COVID-19 immunisation, Lip oedema, Feeling abnormal, Loss of consciousness, Dyspnoea, Oropharyngeal discomfort, Ventricular extrasystoles, Muscular weakness, White blood cell count increased, Toothache, Blood pressure increased, Vaccination site mass, Sinus tachycardia, Erythema, Malaise, Fatigue, Vaccination site pain, and Hypersensitivity.

Case Number	Country of Incidence	Patient Age	Patient Sex	Preferred Term/s with Reported Verbatim	Seriousness	Case Summary
4.1(b) [redacted]	4.1(b)	54 Years	Female	Blood pressure increased (High blood pressure); Visual impairment (Decreased vision); Skin burning sensation (Burning head); Vision blurred (Blurred vision); Injection site haematoma (Hematoma in the arm); Flushing (Redness of the face and neck); Diarrhoea (Diarrhea); Hypertensive crisis (Hypertensive crisis); Lymphadenopathy (Swollen lymph nodes in the ears); Pyrexia (Fever); Vomiting (Vomit); Headache (Headache); Nausea (Nausea)	Hospitalisation	A 54-year old female was vaccinated with intramuscular Nuvaxovid. Medical history was reported as allergy to allopathic drugs. She experienced Blood pressure increased, Visual impairment, Skin burning sensation, Vision blurred, Injection site haematoma, Flushing, Diarrhoea, Hypertensive crisis, Lymphadenopathy, Pyrexia, Vomiting, Headache, and Nausea. At the time of reporting the outcome for all events was recovering/resolving.

- Conclusion

Based on Eudravigilance Data Analysis System (EVDAS) eRMR (n=25, [ROR]=1.31), hypertension was identified as a signal of disproportionate reporting. This underwent a preliminary validation review, based on which, it was not validated due to the low informative value of ICSRs. A summary of this review was presented in SSR No. 05. In addition, it is highly prevalent in the general population in conjunction and with the overall low reporting frequency and given that events of transient blood pressure elevation are expected within the context of vaccination related anxiety. A summary of this review was presented in SSR No. 05

- Potential Immune-Mediated Medical Conditions (PIMMC)

PIMMC is a safety topic under surveillance due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the broad search strategy; SMQ (broad); Immune-mediated \autoimmune disorders.

- Results and discussion

During the reporting interval and cumulatively, the database query identified 82 ICSRs which contained 84 AEs including 20 serious and 1 non-serious, medically confirmed AEs; and 43 serious and 20 non-serious, non-medically confirmed AEs.

There were 63 serious AEs, most of which were coded to PT Pericarditis (n=32) and Myocarditis (n=8). Of the 82 ICSRs, 47 were for females and 35 for males; the age range was 19-76 years. The TTO ranged from 0-50 days when reported (n=51). The majority of AEs were serious, non-medically confirmed (n=43,51.19%). The outcome of most events was not recovered at the time of reporting. Relevant medical history included multiple sclerosis, pericarditis, Crohn's disease, and chest pain. No relevant concomitant medications were reported.

The rr was 7.93 per 100,000 doses administered, equivalent to 0.00793% of all doses administered.

- Conclusion

A review of these reports did not reveal a causal association due to insufficient information. No safety signal was identified.

- Potential interaction concomitant treatments

The global vaccine safety database was queried for interval and cumulative ICSRs using the prespecified search strategy for potential interaction concomitant treatments (refer to Table 42).

- Results and Discussion

During the reporting interval and cumulatively, the database query identified a single ICSR for potential interaction concomitant treatment coded to PT Drug interaction (n=1) with pyridostigmine. This non-serious, non-medically confirmed AE occurred in an adult female. Medical history included myasthenia gravis. No other significant details were reported.

The rr was 0.097 per 100,000 doses administered, equivalent to 0.00010% of all doses administered.

- Conclusion

A review of this report did not identify any trend in potential interaction with concomitant treatments. No safety signal was identified.

Appendix 16: Canada Regional Appendix

This section presents the additional safety topics and requirements for Canada that are not already discussed in the PBRER.

- Number of ICSRs in Canada (Interval and Cumulative)
  During the reporting interval and cumulatively, 7 ICSRs were received from Canada.
- Number of ICSRs Globally (Interval and Cumulative)
  During the reporting interval and cumulatively 1874 ICSRs were reported.
- All ICSRs received globally in the reporting interval and cumulatively stratified by dose, gender and age group are presented below.

Safety Topics for monitoring for Canada

Table 44: Safety Topics and MedDRA Search Strategy for Canada

Safety Topic	MedDRA[a] Search Strategy
PIMMC	SMQ (broad): Immune-mediated/autoimmune disorders
Potential interaction concomitant treatments	PTs: Drug interaction; Inhibitory drug interaction; Potentiating drug interaction; Labelled drug-drug interaction medication error

[a]MedDRA 25.0

The topics of vaccination errors and vaccination failures (refer to Appendix 14 for search strategy) were not included below as these are discussed in Section 9.2 and Section 16.3.5 respectively.

- Potential Immune-Mediated Medical Conditions (PIMMC)

PIMMC is a safety topic under surveillance due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the broad search strategy; SMQ (broad): Immune-mediated/autoimmune disorders.

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 82 ICSRs which contained 84 AEs including 20 serious and 1 non-serious, medically confirmed AEs; and 43 serious and 20 non-serious, non-medically confirmed AEs...

There were 63 serious AEs, most of which were coded to PT Pericarditis (n=32) and Myocarditis (n=8). Of the 82 ICSRs, 47 were for females and 35 for males; the age range was 19-76 years. The TTO ranged from 0-50 days when reported (n=52). The majority of AEs were serious, non-medically confirmed (n=43,51.19%). The outcome of most events was not recovered at the time

of reporting. Relevant medical history included multiple sclerosis, pericarditis, Crohn's disease, and chest pain. No relevant concomitant medications were reported.

The rr was 7.93 per 100,000 doses administered, equivalent to 0.00793% of all doses administered.

- Conclusion

A review of these reports did not reveal a causal association due to insufficient information. No safety signal was identified.

- Potential interaction concomitant treatments

Potential interaction concomitant treatments is a safety topic under surveillance to monitor any trends in vaccine-drug interactions within the post-marketing setting.

The global vaccine safety database was queried for interval and cumulative ICSRs using the prespecified search strategy for potential interaction concomitant treatments (refer to Table 44).

- Results and Discussion
- During the reporting interval and cumulatively, the database query identified a single ICSR for potential interaction concomitant treatment coded to PT Drug interaction (n=1) with pyridostigmine. This non-serious, non-medically confirmed AE occurred in an adult female. Medical history included myasthenia gravis. No other significant details were reported.
- The rr was 0.097 per 100,000 doses administered, equivalent to 0.00010% of all doses administered.
- Conclusion

A review of this report did not identify any trend in potential interaction with concomitant treatments. No safety signal was identified.

COVID-19 VACCINE 20-Dec-2021 to 19-Jun-2022

Canada Specific Report (ICSRs reported globally)

Country	Dose Count	Patient Age Group	Patient Pregnant ?	Male				Female				Unknown			
				SER		NS		SER		NS		SER		NS	
				(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)
CANADA	1	5. Adult	N/A	1	1	1	1	0	0	0	0	0	0	0	0
			Unknown	0	0	0	0	0	0	1	1	0	0	0	0
			Subtotal	**1**	**1**	**1**	**1**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**
		6. Elderly	No	0	0	0	0	0	0	2	2	0	0	0	0
			Subtotal	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**2**	**0**	**0**	**0**	**0**
		Unknown	No	0	0	0	0	0	0	1	1	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	1	1
			Subtotal	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**1**	**1**
		Subtotal		**1**	**1**	**1**	**1**	**0**	**0**	**4**	**4**	**0**	**0**	**1**	**1**
	Subtotal			**1**	**1**	**1**	**1**	**0**	**0**	**4**	**4**	**0**	**0**	**1**	**1**
GLOBAL	1	3. Child	N/A	0	0	1	1	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	1	1
			Subtotal	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**
		4. Adolescent	N/A	0	0	7	7	0	0	0	0	0	0	0	0
			Unknown	0	0	0	0	0	0	3	3	0	0	0	0
			Subtotal	**0**	**0**	**7**	**7**	**0**	**0**	**3**	**3**	**0**	**0**	**0**	**0**
		5. Adult	N/A	91	91	340	340	0	0	2	2	0	0	0	0
			No	0	0	0	0	0	0	4	4	0	0	0	0
			Unknown	0	0	0	0	165	165	751	751	0	0	7	7
			Yes	0	0	0	0	3	3	0	0	0	0	0	0
				0	0	0	0	15	15	84	84	1	1	7	7
			Subtotal	**91**	**91**	**340**	**340**	**183**	**183**	**841**	**841**	**1**	**1**	**14**	**14**
		6. Elderly	N/A	11	11	23	23	0	0	1	1	0	0	0	0
			Unknown	0	0	0	0	17	17	65	65	0	0	1	1
				0	0	0	0	0	0	4	4	1	1	3	3
			Subtotal	**11**	**11**	**23**	**23**	**17**	**17**	**70**	**70**	**1**	**1**	**4**	**4**

COVID-19 VACCINE 20-Dec-2021 to 19-Jun-2022

Canada Specific Report (ICSRs reported globally)

Country	Dose Count	Patient Age Group	Patient Pregnant ?	Male				Female				Unknown			
				SER		NS		SER		NS		SER		NS	
				(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)
GLOBAL	1	Unknown	N/A	4	4	23	23	0	0	0	0	0	0	0	0
			Unknown	0	0	0	0	8	8	46	46	0	0	1	1
				0	0	0	0	0	0	2	2	0	0	3	3
			Subtotal	**4**	**4**	**23**	**23**	**8**	**8**	**48**	**48**	**0**	**0**	**4**	**4**
		Subtotal		**106**	**106**	**394**	**394**	**208**	**208**	**962**	**962**	**2**	**2**	**23**	**23**
	2	5. Adult	N/A	7	7	36	36	0	0	0	0	0	0	0	0
			Unknown	0	0	0	0	10	10	79	79	0	0	0	0
			Yes	0	0	0	0	1	1	0	0	0	0	0	0
				0	0	0	0	1	1	6	6	0	0	1	1
			Subtotal	**7**	**7**	**36**	**36**	**12**	**12**	**85**	**85**	**0**	**0**	**1**	**1**
		6. Elderly	N/A	2	2	4	4	0	0	0	0	0	0	0	0
			Unknown	0	0	0	0	3	3	6	6	0	0	0	0
				0	0	0	0	0	0	1	1	0	0	0	0
			Subtotal	**2**	**2**	**4**	**4**	**3**	**3**	**7**	**7**	**0**	**0**	**0**	**0**
		Unknown	N/A	0	0	4	4	0	0	0	0	0	0	0	0
			Unknown	0	0	0	0	0	0	3	3	0	0	1	1
				0	0	0	0	0	0	2	2	0	0	1	1
			Subtotal	**0**	**0**	**4**	**4**	**0**	**0**	**5**	**5**	**0**	**0**	**2**	**2**
		Subtotal		**9**	**9**	**44**	**44**	**15**	**15**	**97**	**97**	**0**	**0**	**3**	**3**
	3	5. Adult	Unknown	0	0	0	0	0	0	1	1	0	0	0	0
			Subtotal	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**
		Subtotal		**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**
	4	6. Elderly	N/A	0	0	0	0	0	0	1	1	0	0	0	0
			Subtotal	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**
		Subtotal		**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**
	6	Unknown	Unknown	0	0	0	0	1	1	0	0	0	0	0	0
			Subtotal	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**
		Subtotal		**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**

COVID-19 VACCINE 20-Dec-2021 to 19-Jun-2022

Canada Specific Report (ICSRs reported globally)

Country	Dose Count	Patient Age Group	Patient Pregnant ?	Male				Female				Unknown			
				SER		NS		SER		NS		SER		NS	
				(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)	(int)	(Cum)
GLOBAL	8	Unknown	N/A	1	1	0	0	0	0	0	0	0	0	0	0
			Subtotal	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
		Subtotal		**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
	Subtotal			**116**	**116**	**438**	**438**	**224**	**224**	**1,061**	**1,061**	**2**	**2**	**26**	**26**
Total				**117**	**117**	**439**	**439**	**224**	**224**	**1,065**	**1,065**	**2**	**2**	**27**	**27**

Appendix 17: EU Regional Appendix

The number of reports per EU country received during the reporting interval and cumulatively are presented in Table 45.

Table 45: Number of Reports per EU Country Received During the Reporting Interval and Cumulatively

EU Country	Interval				Cumulative			
	Medically Confirmed		Non-Medically Confirmed		Medically Confirmed		Non-Medically Confirmed	
	SER	NS	SER	NS	SER	NS	SER	NS
Austria	2	1	10	17	2	1	10	17
Belgium	1	0	5	5	1	0	5	5
Croatia	2	0	0	0	2	0	0	0
Czech Republic	0	0	1	8	0	0	1	8
Estonia	0	0	1	0	0	0	1	0
Finland	3	1	2	3	3	1	2	3
France	7	10	5	33	7	10	5	33
Germany	11	20	113	588	11	20	113	588
Greece	1	0	2	0	1	0	2	0
Ireland	1	0	3	0	1	0	3	0
Italy	7	13	25	84	7	13	25	84
Lithuania	0	0	0	1	0	0	0	1
Luxembourg	1	0	0	2	1	0	0	2
Netherlands	0	0	1	28	0	0	1	28
Slovenia	1	0	0	0	1	0	0	0
Sweden	1	0	2	0	1	0	2	0
Total	38	45	170	769	38	45	170	769

- Safety Topics for monitoring for EU

Table 46: Safety Topics and MedDRA Search Strategy for EU

Safety Topic	MedDRA[a] Search Strategy
Safety effects of mixed schedules	PTs: Extra dose administered; Inappropriate schedule of product administration; Inappropriate schedule of product discontinuation; Incomplete course of vaccination; Incorrect product administration duration; Incorrect product formulation administered; Interchange of vaccine products; Off-label use; Product administration interrupted; Product dose omission in error; Product dose omission issue; Product substitution; Product substitution error; Product substitution issue; Routine immunisation schedule incomplete; Routine immunisation schedule not administered; Unknown schedule of product administration; Unknown vaccine product administered; Wrong schedule

[a]MedDRA 25.0

- Safety Effects of Mixed Schedules

Safety effects of mixed schedules is a safety topic under surveillance to monitor any trends in the post-marketing setting.

The global vaccine safety database was queried for interval and cumulative ICSRs using the prespecified search strategy for safety effects of mixed schedules (refer to Table 46).

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 25 ICSRs which contained a total of 34 AEs. One report of off-label use was in a 9-year-old child and hence was omitted from this assessment as it did not pertain to safety effects of mixed schedules. After excluding this ICSR, 24 ICSRs were retrieved which contained 33 AEs coded to PTs Off label use (n= 15), Interchange of vaccine products (n=8), Incomplete course of vaccination (n=5), Inappropriate schedule of product administration (n=4) and Extra dose administered (n=1). The majority of ICSRs were reported as non-medically confirmed and non-serious (n=17, 71%).

Of the 24 ICSRs, 14 were for females with age ranging from 25 to ‘late 70s’, 8 for males with age ranging from 32-56 years and 2 individuals with unspecified gender were in late 70s.

NVX-CoV2373 was given as heterologous booster after two doses of Spikevax in one ICSR which was serious, non-medically confirmed, and involved hospitalisation. The 32-year-old male in this report had experienced shaking, chills, anxiety, and chest pain following second dose of Spikevax. Three hours after booster dose NVX-CoV2373, he was hospitalised due to chest pain, nausea and anxiety. All these events except nausea were reported as recovered at the time of reporting. In 3 ICSRs, NVX-CoV2373 was given as a heterologous booster dose after receiving 2 doses of AstraZeneca COVID-19 vaccine. No associated AEs were identified in these reports.

In 4 ICSRs, NVX-CoV2373 was given as heterologous dose after receiving either of the following vaccines as previous doses; Comirnaty (COVID-19 vaccine, mRNA), Spikevax, AstraZeneca COVID-19 vaccine, and Janssen COVID-19 vaccine. One ICSR identified a male of unspecified gender who had 4 mixed doses of Comirnaty and Spikevax before the administration of NVX-CoV2373. No associated AEs were reported in these 4 ICSRs except for one ICSR which included previous dosing with Comirnaty and reported the AE of chest pain (n=1), two days after administration of NVX-CoV2373.

The rr (based on the 24 ICSRs) was 2.32 per 100,000 doses administered, equivalent to 0.00232% of all doses administered.

- Conclusion

A review of these reports did not suggest any trend in safety profile of mixed schedules. No safety signal was identified.

Appendix 18: UK Regional Appendix

The UK specific annex for safety topics that are not already discussed in the PBRER are discussed below in Table 47.

Table 47: Safety Topics and MedDRA Search Strategy for the UK

Safety Topic	MedDRA[a] Search Strategy
PIMMC	SMQ (broad): Immune-mediated/autoimmune disorders
Age group: Paediatrics	Review of safety concerns in individuals < 18

[a]MedDRA 25.0

- Off-label Paediatric Use

Off-label paediatric use is under surveillance to monitor the safety of the vaccine in this population.

The global vaccine safety database was queried for the cumulative period up to 19-Jun-2022 to include all ICSRs involving paediatric patients <18 years of age.

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 12 ICSRs of off-label paediatric use which contained 25 AEs including 3 non-serious, medically confirmed AEs; and 22 non-serious, non-medically confirmed AEs. Of the 25 AEs, the most frequently reported PTs included Product administered to patient of inappropriate age (n=8), and Vaccination error (n=11). The majority of AEs were non-medically confirmed and non-serious (n=22, 88%). The outcome of majority of events were reported as recovered at the time of reporting.

Of the 12 ICSRs, 3 were for females, 8 for males and 1 was of an unknown gender; the age range was 9-17 years. No significant medical history or concomitant medications were reported for the ICSRs.

The PTs are presented in Table 48.

The rr was 1.16 per 100,000 doses administered, equivalent to 0.00116% of all doses administered.

Table 48: AEs Reported for Off-Label Paediatric Use

MedDRA PT Age Groups	Cumulative			
	Medically Confirmed		Non-Medically Confirmed	
	Serious	Non-Serious	Serious	Non-Serious
Child				
Vaccination error	0	0	0	1
Off label use	0	1	0	0
Adolescent				
Injection site pain	0	0	0	2
Vaccination error	0	1	0	9
Product administered to patient of inappropriate age	0	1	0	7
Wrong product administered	0	0	0	3
Total	**0**	**3**	**0**	**22**

- Conclusion

A review of these reports did not suggest any trends in AEs particular to this population compared to the AE profile as defined in the CCDS for the overall population. No safety signal was identified.

- Potential Immune-Mediated Medical Conditions (PIMMC)

PIMMC is a safety topic under surveillance due to insufficient information obtained from clinical studies.

The global vaccine safety database was queried for interval and cumulative ICSRs using the broad search strategy; SMQ (broad): Immune-mediated/autoimmune disorders.

- Results and Discussion

During the reporting interval and cumulatively, the database query identified 82 ICSRs which contained 84 AEs. There included 20 serious and 1 non-serious, medically confirmed AEs; and 43 serious and 20 non-serious, non-medically confirmed AEs.

There were 63 serious AEs, most of which were coded to PT Pericarditis (n=32) and Myocarditis (n=8). Of the 82 ICSRs, 47 were for females and 35 for males; the age range was 19-76 years. The TTO ranged from 0-50 days when reported (n=52). The majority of AEs were serious, non-medically confirmed (n=43, 51.19%). The outcome of most events was not recovered at the time of reporting. Relevant medical history included multiple sclerosis, pericarditis, Crohn's disease, and chest pain. No relevant concomitant medications were reported. The outcome of most events was not recovered at the time of reporting.

The rr was 7.93 per 100,000 doses administered, equivalent to 0.00793% of all doses administered.

- Conclusion

A review of these reports did not reveal a causal association due to insufficient information. No safety signal was identified.

Appendix 19: Line Listing of Fatal Cases

COVID-19 VACCINE 20-Dec-2021 to 19-Jun-2022

Interval Line Listing of Fatal Cases

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 01-JUN-22 1) 03-JUN-22 2) 08-JUN-22	AUSTRALIA	Elderly	NUVAXOVID / Injection	UNK: 01-APR-2022	Concomitant disease aggravated			Y	Y	Y
		Regulatory Authority	96	1) Intramuscular	1) -	Fatal					
			Male								

Case Narrative

On 25-MAY-2022, this serious initial regulatory authority safety report from Australia was received from a physician via the Therapeutic Goods Administration (TGA Reference number: 4.1(b) via BioCelect and was received by Novavax on 01-JUN-2022.

The following narrative was provided by the Therapeutic Goods Administration:

Death from CVA post novavax PMHx: AF, T2DM, LEWY BODY DEMENTIA, congestive heart ds, parkinson's, CVA, Previous vaccine reactions: No NA

On 03-JUN-2022, a significant correction was identified with Day 0 of 03-JUN-2022. The following information was updated: The statement "This report is confounded by medical history, and the temporal relationship is unclear." was added to the sender comment.

On 08-JUN-2022, follow-up information was received by Novavax via Therapeutic Goods Administration (TGA reference number: 4.1(b)). Therapeutic Goods Administration (TGA) received the report on 25-MAY-2022. No new information was received.

Total Row Count: 1
Total Case Count: 1

Appendix 20: Signal Evaluation Report of Anaphylaxis

COVID-19 Vaccine (Recombinant, Adjuvanted) (NVX-COV2373)

Main Brand Names: NUVAXOVID™

SIGNAL EVALUATION REPORT: ANAPHYLAXIS

Date of Report: 28-JUN-2022

Marketing Authorization Holder:

(NOVAVAX, Inc.)

Electronic signature approval(s) signifies that the approver approves this document as acceptable, accurate, and complete.

DESCRIPTION	NAME / TITLE	SIGNATURE / DATE
PREPARED BY:	4.1(b) [redacted]	4.1(b) [redacted]
APPROVED BY:	4.1(b) [redacted]	
APPROVED BY:	4.1(b) [redacted]	

EXECUTIVE SUMMARY

Background

Nuvaxovid/Covid-19 Vaccine (recombinant, adjuvanted) (NVX-CoV2373) is indicated for active immunization to prevent Coronavirus Disease-19 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals aged 18 years of age and older (authorised as COVOVAX in India and Thailand for ages > 12 and < 18 years).

NUVAXOVID is a purified full-length SARS-CoV-2 recombinant spike (S) protein that is stabilised in its prefusion conformation. The addition of the saponin-based Matrix-M™ adjuvant facilitates activation of the cells of the innate immune system, which enhances the magnitude of the S protein-specific immune response. The 2 vaccine components elicit B- and T-cell immune responses to the S protein, including neutralising antibodies, which may contribute to protection against COVID-19.

Anaphylaxis is a severe, potentially life-threatening, systemic allergic reaction that occurs acutely after contact with a substance that triggers an immunologic reaction[1]. Most anaphylactic reactions are considered to be mediated by IgE, immunoglobulins interacting with antigenic molecules, any component of a vaccine, including antigen and excipients can be implicated in allergic reactions, including anaphylaxis.

Worldwide Market Authorization Status

On 20-Dec-2022, the first marketing authorization (MA) for Nuvaxovid was granted in European Union which is considered to the be International Birthdate (IBD).

Current CCDS/Labeling Status

Anaphylaxis is an important potential risk in the Nuvaxovid RMP from the time of first marketing authorization. The current Company Core Data Sheet (CCDS) section 4.4 Warnings and Precautions states that “events of anaphylaxis have been reported with COVID-19 vaccines.” Anaphylaxis following vaccination with Nuvaxovid is not described in CCDS version 3.0 (effective date 03-May-2022).

Sources of Signal

Health Authority Request
On 18-May-2022 a request for label update was received from the Therapeutic Goods Administration (TGA) and a signal of anaphylaxis was validated. The request was to update the Product Information section 4.4 (Special Warnings and Precautions for Use) and section 4.8 (Adverse Effects).

Clinical Trial Data

No events of anaphylaxis have been reported in the pooled analysis of safety data in adult participants from the start of first vaccination through the data extraction dates of the respective clinical studies (28-Jul-2021 for 2019nCoV-101 Part1, 11-Jun-2021 for

2019nCoV-101 Part2, 04-Oct-2021 for2019nCoV-302, 27-Oct-2021 for /2019nCoV-501and 20-Jan-2022 for 2019nCoV-301). Thus, no signal of anaphylaxis was identified during the clinical development program.

Post-marketing Observed/Expected and Signal of Disproportionate Reporting Data

An Observed vs Expected analysis (20-Dec-2021 to 12-May-2022) revealed an increased observed-to-expected rate for the Adverse Event of Special Interest (AESI) of anaphylaxis that was statistically significant. However, when limited to medically confirmed adverse events, this increased rate was not statistically significant.

The MedDRA PT Anaphylaxis became a signal of disproportionate reporting (SDR) based on EudraVigilance Data Analysis System (EVDAS) Electronic Reaction Monitoring Report (eRMR) (16-Mar-2022 to 31-Mar-2022; n=5, ROR=1.46).

Both the crude O/E rate and SDR contribute to signal generation and subsequent validation of the AESI Anaphylaxis.

Objective

The objective of this report is to describe a comprehensive review of the safety data relevant to anaphylaxis from clinical trials and post marketing data and to determine whether the available evidence supports or refutes an association between Nuvaxovid and anaphylaxis.

Methods

Clinical trial data: The clinical trial database was searched using SMQ Narrow Anaphylactic reaction for all adverse event data, pre and post crossover, in studies 2019nCoV-101 Part1, 2019nCoV-101 Part2, 2019nCoV-301, 2019nCoV-302 and 2019nCoV-501 to data extraction dates for the respective clinical studies.

Post market data: The safety database was searched using the Adverse Event of Special Interest (AESI) Anaphylaxis search strategy for all cases up to 21-May-2022. The search strategy included HLT: Anaphylactic and anaphylactoid responses. These individual case safety reports (ICSRs) were adjudicated against the Brighton Collaboration (BC) case definition for anaphylaxis.

Results

Clinical trial data: There were no events of anaphylaxis reported in Novavax clinical trials.

Post market data: As of the data cut of 21-May-2022, 14 ICSRs were retrieved from the safety database that met the search criteria. Two reports met the case definition for anaphylaxis Level 1 with time to onset of 20 minutes, these 2 ICSRs were determined to be duplicates on 17-Jun-2022. One report was Level 2 with time to onset of 18 hours. The remaining 11 reports were assessed as Level 4, a “report of anaphylaxis with insufficient evidence to meet any level of case definition.”

Conclusion

The signal was confirmed as an important identified risk by the Safety Review Team (SRT) on 27 June 2022.

Safety Review Team Recommendation/Endorsement

The SRT endorsed TGA requested updates to local Australian Product Information Section 4.4 (Special Warnings and Precautions for Use) and Section 4.8 (Adverse Effects). The SRT further recommended an update to the CCDS to include NUVAXOVID in the current general warning and precautions statement regarding anaphylaxis in alignment with the local label update.

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LIST OF ABBREVIATIONS

Acronym	Abbreviation Definition
AESI	Adverse Event of Special Interest
BC	Brighton Collaboration
BP	Blood Pressure
CCDS	Company Core Data Sheet
DAEN	Database of Adverse Event Notifications (Australia)
DLP	Data Lock Point
E	Expected
eRMR	Electronic Reaction Monitoring Report
EVDAS	EudraVigilance Data Analysis System
F	Fatal
GERD	Gastro Esophageal Reflux Disease
HR	Hour
ICSR	Individual Case Safety Report
Min	minutes
NVX	Novavax
PT	MedDRA Preferred Term
ROR	Reporting Odd Ratio
SRT	Safety Review Team
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SDR	Signal of Disproportionate Reporting
SOB	Shortness Of Breath
TGA	Therapeutic Good Administration (Australia)
SPEAC	Safety Platform For Emergency Vaccine
TTO	Time to onset

1 INTRODUCTION

This signal evaluation report provides a detailed analysis on the validated safety signal of anaphylaxis in association with the administration of Nuvaxovid indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older.

2 WORLDWIDE MARKET AUTHORIZATION STATUS

On 20-Dec-2022, the first marketing authorization (MA) for Nuvaxovid was granted in European Union which is considered to the be International Birthdate (IBD).

3 SOURCE OF THE SIGNAL

On 18-May-2022 a request for label update for anaphylaxis from Therapeutic Good Administration (TGA), Australia was received and the signal was validated. The request was to update the Product Information section 4.4 (Special Warnings and Precautions for Use) and section 4.8 (Adverse Effects).

4 BACKGROUND

Anaphylaxis is a severe, potentially life-threatening, systemic allergic reaction that occurs acutely after contact with a substance that triggers an immunologic reaction[1]. Most anaphylactic reactions are considered to be mediated by IgE, immunoglobulins interacting with antigenic molecules. Any component of a vaccine, including antigen and excipients can be implicated in allergic reactions, including anaphylaxis.

Anaphylaxis is listed in Section 4.4 of the NUVAXOVID Company Core Safety Information (CCSI) as a general warning and precaution related to COVID-19 vaccines. It is currently an important potential risk and an adverse event of special interest for continuous monitoring under the NUVAXOVID pharmacovigilance plan.

5 EXPECTED VS OBSERVED DATA

The list of selected background rate per AESI countries included Australia, Canada, Europe, New Zealand and South Korea. The risk window identified for Anaphylaxis was 0 to 7 days. The TTO for 8 reports were unknown. One of the 11 reports fell outside the risk window. Reports with missing time window are conservatively included in the analysis. Therefore 10 reports were included in the overall analysis.

When accounting for all cumulative Anaphylaxis AESI reports meeting inclusion criteria (medically and non-medically confirmed), the crude observed rate as reported, showed an increase when compared to the expected rate with a statistically significant rate ratio (RR) of 2.81 (95% confidence interval [CI] of 1.35 – 5.17). When assuming a 50% underreporting rate, the results were similar with an RR of 5.62 (95% CI: 2.70 – 10.33). Similar results were obtained when assuming 75% underreporting with an RR of 11.23 (95% CI: 5.40 – 20.66).

When only medically confirmed reports meeting inclusion criteria were considered (n=5), observed rates were increased but not statistically significant except at 75% under reporting where the O/E rate ratio was 5.61 (95% Cl: 1.82 – 13.11).

6 METHODS

6.1 Search Strategy

6.1.1 Clinical Studies

The clinical trial database was searched using SMQ Narrow Anaphylactic reaction.
Pre-crossover study and data cut dates are as follows: 2019nCoV-101 Part1 as of 28-Jul-2021, 2019nCoV-101 Part2 as of 11-Jun-2021, 2019nCoV-302 as of 27-Jul-2021, 2019nCoV-501 as of 27-Oct-2021, and 2019nCoV-301 as of 17-Feb-2022.
Post-crossover study and data cut dates are as follows: 2019nCoV-301 as of 17-Feb-2022, and 2019nCoV-302 as of 27-Jul-2021.

6.1.2 Post-marketing Database

The ARGUS safety database was searched using the Adverse Event of Special Interest (AESI) Anaphylaxis search strategy for all cases up to 21-May-2022. The search strategy included the following: HLT: Anaphylactic and anaphylactoid responses. PTs from this HLTs are presented in Appendix 1 SEARCH TERMS.

6.2 Analysis Strategy

Case Definition

All post market ICSRs were medically reviewed and adjudicated against the Brighton Collaboration (BC)[2] case definition criteria for anaphylaxis level 1 - 5. Brighton level 1 represents the highest level of diagnostic certainty that a reported case is indeed a case of anaphylaxis; levels 2 and 3 represent successively lower levels of diagnostic certainty. Level 4 is a case reported as anaphylaxis, but which does not meet the Brighton Collaboration case definition. Level 5 is not a case of anaphylaxis.

7 RESULTS

7.1 Analysis of Data from Clinical Studies

As of the respective data extraction dates for the clinical studies for the integrated safety summary, there were no events of anaphylaxis reported in Novavax clinical trials. Refer to Table 1 and Table 2.

Table 1: Summary of Number of Events and the Events Rates for Anaphylactic Reaction (SMQ, Narrow) Reported in Pre-crossover Period

	Vaccine*	Placebo*	Risk Difference
SMQ Preferred Term (# of Events)	(n, rate per 100 person-years, 95% CI) N = 30072	(n, rate per 100 person-years, 95% CI) N = 19877	(Vaccine - Placebo) (rate per 100 person-years, 95% CI)
No Events to Report			

* Treatment group applicable to period. ** Percent calculated based on number of subjects in Safety Analysis set.
Note: At the SMQ level, number of events, event rate, and 95% CI for event rate are presented in first row, with following rows based on participants experiencing events in the SMQ. Risk difference and its Confidence Intervals (CIs) are computed from Mantel-Haenszel Standardized Risk Estimates and 95% normal confidence limits with the stratification by study, while individual group statistics are not adjusted by strata. MedDRA version: 24.0 (2019nCoV-101 Part 1, 2019nCoV-101 Part 2, and 2019nCoV-301), 23.1 (2019nCoV-302), and 23.0 (2019nCoV-501). SMQ version: 24.1. Included study data from 2019nCoV-101 Part1 as of 28JUL2021, 2019nCoV-101 Part2 as of 11JUN2021, 2019nCoV-302 as of 27JUL2021, 2019nCoV-501 as of 27OCT2021, and 2019nCoV-301 as of 17FEB2022. File Name: t_SMQ_pre_crossover_4_1.rtf. Generated from t_smq_pre_crossover.sas 03MAY2022 20:10

Table 2: Summary of Number of Events and the Events Rates for Anaphylactic Reaction (SMQ, Narrow) Reported in Post-crossover Period

	Vaccine*	Placebo*	Risk Difference
SMQ Preferred Term (# of Events)	(n, rate per 100 person-years, 95% CI) N = 9635	(n, rate per 100 person-years, 95% CI) N = 18581	(Vaccine - Placebo) (rate per 100 person-years, 95% CI)
No Events to Report			

* Treatment group applicable to period. ** Percent calculated based on number of subjects in Safety Analysis set.
Note: At the SMQ level, number of events, event rate, and 95% CI for event rate are presented in first row, with following rows based on participants experiencing events in the SMQ. Risk difference and its Confidence Intervals (CIs) are computed from Mantel-Haenszel Standardized Risk Estimates and 95% normal confidence limits with the stratification by study, while individual group statistics are not adjusted by strata. MedDRA version: 24.0 (2019nCoV-301), 23.1 (2019nCoV-302). SMQ version: 24.1. Included study data from 2019nCoV-301 as of 17FEB2022, and 2019nCoV-302 as of 27JUL2021. File Name: t_SMQ_post_crossover_4_1.rtf. Generated from t_smq_post_crossover.sas 03MAY2022 20:20

7.2 Analysis of ICSRs from Post Market Safety Database

Fourteen (14) ICSRs were retrieved from ARGUS safety database, by utilizing the search strategy per section 6.1.2. Demographic data, ICSR country and outcomes are presented in Figure 1 and Figure 2.

All ICSRs were medically reviewed and adjudicated against the Brighton Collaboration (BC)[2] case definition criteria for anaphylaxis levels 1 to 5. Two reports met case definition of anaphylaxis Level 1 with time to onset of 20 minutes; these 2 ICSRs were determined to be duplicates on 17-Jun-2022. One report met Level 2 criteria with time to onset of 18 hours.

The remaining eleven reports were assessed as Level 4, a report of anaphylaxis with insufficient evidence to meet any level of case definition.

The cases meeting BC level 1 and level 2 of diagnostic certainty are presented in Table 3: Cases Meeting Criteria for BC level 1 and 2. The outcomes were recovered, recovering, or unknown. There were no fatalities.

DEMOGRAPHICS (n=14)

Figure 1: Post Market ICSRs Age and Sex Distribution

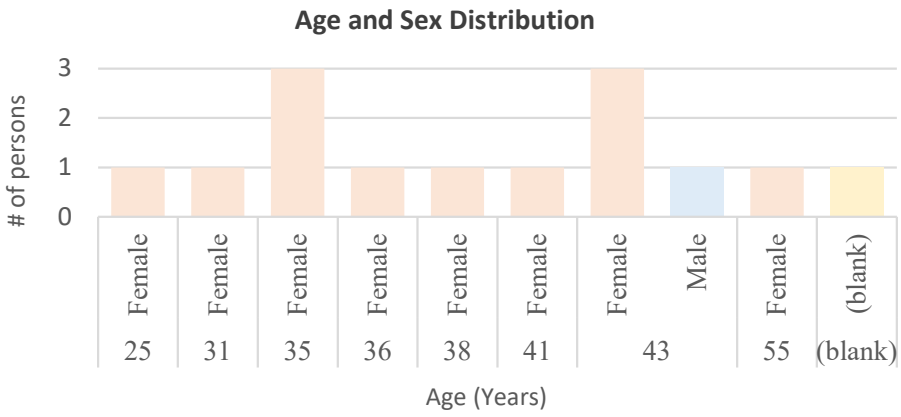
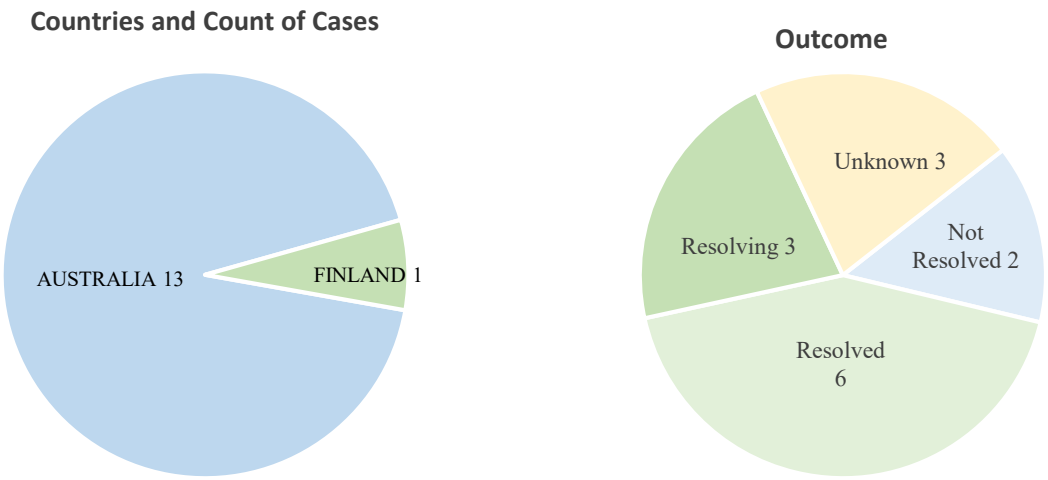


Figure 2: Post Market Count of ICSRs Countries and Outcome



CASES

Table 3: Cases Meeting Criteria for BC level 1 and 2

Case Number	Brief Narrative	Symptoms	Preferred Term	Outcome	TTO	Allergic History	Treatment	Level[2]	Brighton Criteria[2]
4.1(b)	A 35-year-old female, with a history of anaphylaxis to flu vaccine, experienced an anaphylactic reaction 20 minutes after receiving Nuvaxovid. Her symptoms began with hives and then progressed to include swelling of face, lips and throat, with trouble breathing. She self administered her EpiPen and the event resolved.	hives, then swelling of face, lips and throat, with trouble breathing	Anaphylactic reaction	Resolved	20 min	Anaphylaxis post flu vaccine	EpiPen	**1**	Major: Hives, lip, face and throat swelling Minor: Trouble breathing
4.1(b)	A 36-year-old female patient with history of anaphylaxis to flu vaccine experienced an anaphylactic reaction 20 mins after receiving Nuvaxovid. Her symptoms began with hives and then progressed to include swelling of face, lips and throat, with trouble breathing. She administered her EpiPen.	hives, swelling of the face, lips and throat, trouble breathing	Anaphylactic reaction	Unknown	20 min	anaphylaxis post flu vaccine	EpiPen	**1**	Major: Hives, swelling of face: lip, throat Minor: Trouble breathing
4.1(b)	A 25-year-old female experienced bilateral lip swelling, nausea, shortness of breath (SOB), sensation of throat tightening, and mild edema of posterior oropharynx 18 hours after receiving first dose of Nuvaxovid. She had no stridor nor wheeze. She was treated with adrenaline, prednisolone for recurrent symptoms. Post 3rd dose of adrenaline, sustained resolution of symptoms was achieved.	bilateral lip swelling, nausea, SOB, sensation of throat tightening, and mild edema of posterior oropharynx	Anaphylactic reaction	Resolved	18 hr	not reported	adrenaline, prednisolone	**2**	Major: Bilateral lip swelling Minor: Nausea, sensation of throat tightening, SOB

*As of DLP, 21-May-2022: Both 4.1(b) and 4.1(b) were in the database. On 17-Jun-2022, these 2 ICSRs were confirmed to be duplicates.

7.3 Disproportionality Statistics

MedDRA PT Anaphylaxis became a signal of disproportionate reporting (SDR) based on EudraVigilance Data Analysis System (EVDAS) Electronic Reaction Monitoring Report (eRMR) (16-Mar-2022 to 31-Mar-2022; n=5, ROR=1.46).

7.4 Observed vs Expected (O/E) Analysis

An Observed vs Expected analyses (20-Dec-2021 to 12-May-2022) revealed an increased observed rate for the Adverse Event of Special Interest (AESI) of anaphylaxis that was statistically significant and remained so at 50% and 25% sensitivity levels. However, when limited to medically confirmed adverse events, the increase was not statistically significant. MedDRA PT Anaphylaxis became a signal of disproportionate reporting (SDR) based on EudraVigilance Data Analysis System (EVDAS) Electronic Reaction Monitoring Report (eRMR) (16-Mar-2022 to 31-Mar-2022; n=5, ROR=1.46).

8 CONCLUSION

As of the data cut of 21-May-2022, from the post market safety data presented, one case met case definition of anaphylaxis Level 1 with time to onset of 20 minutes, (2 ICSRs were retrieved from the database for Level 1 and determined to be duplicates on 17-Jun-2022). One report met Level 2 criteria with time to onset of 18 hours.

The signal of anaphylaxis is confirmed based on a comprehensive review of the available evidence that supports a causal association between Nuvaxovid and anaphylaxis.

9 SAFETY REVIEW TEAM SIGNAL DISPOSITION

The Australian label sections Product Information section 4.4 (Special Warnings and Precautions for Use) and section 4.8 (Adverse Effects) are planned to be updated per local TGA request. A labeling variation was submitted 22-Jun-2022. The Safety Review Team confirmed anaphylaxis as an identified risk on 27 June 2022. An update to the CCDS will be made to include NUVAXOVID in the current general warning and precautions statement regarding anaphylaxis.

10 REFERENCES

[1] Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF Jr et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol*. 2006;117(2):391.

[2] SPEAC SO2- D2.5.2.1 – AESI Case Definition Companion Guide for 1st Tier AESI Anaphylaxis, V1.0-5-FEB-2021

11 APPENDICES

APPENDIX 1 POST MARKET DATA MEDDRA SEARCH TERMS

Search Strategy HLT: Anaphylactic and Anaphylactoid responses MedDRA version 25.0
PTs under this HLT

MedDRA 25.0 Code	Term	Level
10077535	Anaphylactic and anaphylactoid responses	HLT
10002198	Anaphylactic reaction	PT
10002199	Anaphylactic shock	PT
10067113	Anaphylactic transfusion reaction	PT
10002216	Anaphylactoid reaction	PT
10063119	Anaphylactoid shock	PT
10067010	Anaphylactoid syndrome of pregnancy	PT
10076665	Dialysis membrane reaction	PT

Appendix 21: Signal Evaluation Report of Myocarditis/Pericarditis

Post DLP, the signal disposition status for myocarditis/pericarditis has been reassessed from indeterminate to confirmed.

SAFETY SIGNAL EVALUATION REPORT FOR

Myocarditis and Pericarditis with Use of NUVAXOVID™ DISPERSION FOR INJECTION COVID-19 VACCINE (RECOMBINANT, ADJUVANTED) (NVX-COV2373)

Date of Report: 07-JUL-2022

Marketing Authorization Holder:

(NOVAVAX, Inc.)

Electronic signature approval(s) signifies that the approver approves this document as acceptable, accurate, and complete.

DESCRIPTION	NAME / TITLE	SIGNATURE / DATE
PREPARED BY: 4.1(b)	4.1(b)	4.1(b)
APPROVED BY: 4.1(b)	4.1(b)	
APPROVED BY: 4.1(b)	4.1(b)	

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LIST OF ABBREVIATIONS

Acronym	Abbreviation Definition
AE	Adverse Event(s)
AESI	Adverse Events of Special Interest
BC	Brighton Collaboration
CCDS	Company Core Data Sheet
DLP	Data lock point
EKG	Electrocardiogram
EU	European Union
GP	General practitioner
HLT	High Level Term
ICSR	Individual Case Safety Report
LP	License Partner
MedDRA	Medical Dictionary for Regulatory Activities
N/A	Not applicable
NVX	Novavax
O/E	Observed vs. Expected
PI	Product Information
PT	Preferred Term
PVP	Pharmacovigilance Plan
RMP	Risk Management Plan
SMC	Signal Management Committee
SMQ	Standardised MedDRA Query
SSR	Summary Safety Report
UNK	Unknown

1 INTRODUCTION

This signal evaluation report provides a detailed analysis on the validated safety signal of myocarditis and pericarditis in association with the administration of NUVAXOVID™ COVID-19 Vaccine (recombinant, adjuvanted) (NVX-CoV2373; hereafter referred to as NUVAXOVID) based on the information available to Novavax, Inc. (NVX).

NUVAXOVID is a recombinant, adjuvanted protein vaccine indicated for active immunisation to prevent Coronavirus Disease-19 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals aged 18 years of age and older (authorised as COVOVAX in India and Thailand for ages > 12 and < 18 years). Further details on the mechanism of action, indications, pharmaceutical form(s), and instructions for use are presented in the Company Core Data Sheet (CCDS). The International Birth Date (IBD) of NUVAXOVID is 20-Dec-2021 in the European Union (EU).

2 SOURCE OF THE SIGNAL

The safety signal of myocarditis and pericarditis was identified by signal surveillance activity and Health Authority request. Specifically, the Signal Management Committee (SMC) at NVX validated the signal of myocarditis and pericarditis on 05 May 2022 based on review of the increasing number of ICSRs being reported for myocarditis and pericarditis arising from the Australian TGA DAEN database and statistically significant results of observed vs. expected (O/E) analyses which showed an increase in the observed reporting rate when compared to the expected rate.

On 24 May 2022, the US Food and Drug Administration requested that the pharmacovigilance plan (PVP) be updated to amend the risk of myocarditis and pericarditis from an “Important Potential Risk” to an “Important Identified Risk.” Subsequently, on 27 May 2022, the European Medicines Agency in the Pharmacovigilance Risk Assessment Committee (PRAC) Rapporteur Preliminary Assessment Report for the 3rd Monthly Safety Update requested that myocarditis and pericarditis be classified as signals in the next monthly Summary Safety Report (SSR).

To evaluate and further characterize this signal, a comprehensive review of the safety data relevant to myocarditis and pericarditis from clinical trials and the post-marketing safety database was performed to determine whether the available evidence supports or refutes a causal association between NUVAXOVID and myocarditis and pericarditis.

3 BACKGROUND

3.1 Background Related to Myocarditis and Pericarditis

Myocarditis and pericarditis are uncommon inflammatory heart conditions and may rarely be associated with poor outcomes or death.[1] Clinical presentation may present acutely, or in a subacute or chronic timeframe, with variable involvement of the myocardium and pericardium, from patchy involvement to diffuse involvement of tissue. Multiple infectious triggers have been implicated, including viral, bacterial, parasitic infections, and non-

infectious etiologies include directly cardiotoxic injury e.g., alcohol, cocaine, or radiation, or with systemic diseases such as sarcoidosis, inflammatory bowel disease, etc. In resource-rich countries, acute myocarditis is most commonly associated with viral infections, including parvovirus B19, human herpes virus 6, Coxsackie B, adenovirus, enterovirus, human immunodeficiency virus, cytomegalovirus, and varicella. Recently, recognition through clinical case reports and post-autopsy findings of inflammatory heart disease in patients with COVID-19 illness supports an association of SARS CoV-2 infection with myocarditis and pericarditis.[1, 2]

Historically, post-vaccination myocarditis has been reported after smallpox (59%), anthrax (23%), and typhoid (13%) and inactivated influenza vaccines (11%).[3] Reports of myocarditis and pericarditis temporally associated with COVID-19 vaccination have been described in adults (see Section 3.2). . In a meta-analysis of patients with post-mRNA COVID vaccination, the most common clinical presentation was chest pain (90.7%), followed by dyspnea. Abnormal ECG findings were found in >80%, including ST segment elevation in 68.6%. Other common diagnostic findings include elevated markers of myocardial injury e.g., troponin, echocardiographic evidence of pericardial effusion, ventricular wall thickening or global or regional ventricular wall dysfunction.[4] The clinical course of post-vaccination myopericarditis is generally mild or moderate with complete resolution of symptoms in most, with rates of less than 10% admitted to ICU described in the meta-analysis, and two deaths occurring (2.3%).[5]

The etiology of any possible association between NUVAXOVID and myocarditis/pericarditis has not been established. Myocarditis and pericarditis are considered important potential risks in the Nuvaxovid NUVAXOVID Risk Management Plan (RMP) and PVP.

3.2 Epidemiology

Clusters of myocarditis after mRNA COVID-19 vaccination were first identified as a signal in clinical practice and reporting from passive surveillance systems. Large observational comparative cohort studies conducted in various countries (US, UK, Israel, Denmark, etc.) confirmed the increased risk of myocarditis after mRNA COVID-19 vaccination.[6,7,8,9] It is consistently reported that the risk of myocarditis is higher after the 2nd dose of mRNA vaccination than after the 1st dose, higher in males than in females, and higher in younger ages than older ages.[6,10] The highest risk has been reported in young males ages 12-17 years. The highest period of risk for myocarditis occurs in the 7-day periods after vaccination.[11] Interestingly, a systematic review comparing recipients of COVID-19 vaccines and non-COVID-19 vaccines (smallpox, influenza, yellow fever, OPV, MMR, DPT, and meningococcal) did not identify a difference in the overall incidence of myopericarditis after vaccination; In addition, myocarditis is more likely to occur after receiving mRNA COVID-19 vaccines than after receiving non-mRNA COVID-19 vaccine.[12,13]

The literature suggests that the background rates of myocarditis were elevated in the COVID-19 pandemic period compared to pre-pandemic due to increased risk of myocarditis following SARS-CoV-2 infection or COVID-19. Increased counts of inpatient encounters for myocarditis were observed in the pre-vaccine pandemic period than before pandemic.[14]

Associations between SARS-CoV-2 infection or COVID-19 and myocarditis have been demonstrated globally through large cohort studies in the US (RR=15.7), [14] Israel (RR=18.3),[8] and four Nordic countries (age/sex specific IRRs range from 3.0-15.4).[13] The incidence of myocarditis has been shown to be higher after SARS-CoV-2 infection compared with COVID-19 vaccination.[15] The trend of higher risk of myocarditis after COVID-19 infection being consistently higher than that after receiving a COVID-19 vaccine is consistent across different age groups and in both males and females, respectively.[15] Moreover, myocarditis after natural viral infection appears to be more severe than myocarditis after COVID-19 vaccination with respect to fulmination, mortality, disease duration, and proportions of cardiac dysfunction and functional recovery.[16]

There is little data comparing myocarditis before and during the COVID-19 pandemic. A report found myocarditis increased after the COVID-19 pandemic, and peaks in myocarditis inpatient encounters were generally aligned with peaks in COVID-19 inpatient encounters during April 2020 to January 2021, and both decreased when COVID-19 vaccines became available in the US.[14] More studies are needed to compare the myocarditis disease burden before and during the COVID-19 pandemic over time, particularly in the periods with and without COVID-19 vaccines available, to tease apart the relative contribution of COVID-19 and vaccines on the burden of myocarditis. Of course, the enhanced surveillance and public awareness in the context of COVID-19 vaccination may lead to overreported myocarditis in the era of COVID-19 vaccination.[12] Even so, the benefits of COVID-19 vaccination still substantially outweigh the risks for COVID-19 vaccination in all populations, including adolescents and young adults reported with the highest risk of myocarditis after mRNA COVID-19 vaccination.[17]

3.3 Labeling

CCDS: Currently, myocarditis and pericarditis are considered emerging signals, and are not included in the CCDS.

Health Canada Monograph: Section 8.2: Myocarditis was identified in two teenage men shortly after receiving a second dose of vaccine resulting in a mild clinical course with complete resolution and no sequelae. Currently available information is insufficient to determine a causal relationship with the vaccine.

Australia and New Zealand PIs: Section 4.4: Pericarditis has been spontaneously reported during post authorization use of NUVAXOVID. As these reactions were derived from spontaneous reports, the frequencies could not be determined and are thus considered as not known.

4 EXPOSURE DATA

4.1 Cumulative Subject Exposure in Clinical Trials

Cumulatively, 30,072 adult subjects were administered NUVAXOVID and 19,877 were administered placebo in the integrated pre-crossover (placebo controlled) safety analysis set.

An additional 9,635 adult subjects were administered NUVAXOVID in the post-crossover periods. A total of 1,487 adolescent subjects were administered NUVAXOVID and 745 in the pre-crossover period.

Subjects were exposed in the following clinical trials:

- 2019nCoV-101 Part 1
- 2019nCoV-101 Part 2
- 2019nCoV-301
- 2019nCoV-301 Adolescent Expansion
- 2019nCoV-302
- 2019nCoV-501

4.2 Cumulative Exposure Data from Post-Authorization Experience

Exposure data are derived from administration records and distribution data. Table 1 below lists regional sources of administration and distribution data, including cut-off dates. Administration data stratified by region are provided in Table 2. Distribution data are provided for all regions that received NUVAXOVID and COVOVAX, including some regions where administration data are also available.

Table 1 Administration and Distribution Source Data by Country

Country	Administration Data Source	Administration Data Cut-Off Date	Distribution Data Source	Distribution Data Cut-off Date
Australia[a]	COVID19VaccineData@Health.gov.au	01-Jun-2022	Novavax Global Sales	01-Jun-2022
Canada[a]	https://health-infobase.canada.ca/covid-19/vaccination-coverage/#a6	01-Jun-2022[c]	Novavax Global Sales	01-Jun-2022
EU[a]	https://www.ecdc.europa.eu/en/publications-data/data-covid-19-vaccination-eu-eea	01-Jun-2022[c]	Novavax Global Sales	01-Jun-2022
New Zealand[a]	New Zealand Ministry of Health (NZ MoH) provided by license partner (LP), Biocelect, via Biointelect.	31-May-2022	Novavax Global Sales	01-Jun-2022
Bangladesh[b]	http://103.247.238.92/webportal/pages/covid19-vaccination-update.php	N/A	SIIPL's SSR 08 (01-May-2022 to 31-May-2022)	N/A
India[b]	N/A	N/A	SIIPL's SSR 08	N/A

Table 1 Administration and Distribution Source Data by Country

Country	Administration Data Source	Administration Data Cut-Off Date	Distribution Data Source	Distribution Data Cut-off Date
			(01-May-2022 to 31-May-2022)	
Indonesia[b]	N/A	N/A	SIIPL's SSR 08 (01-May-2022 to 31-May-2022)	31-May-2022
Philippines[b]	https://www.fda.gov.ph/list-of-fda-issued-emergency-use-authorisation/	N/A	SIIPL's SSR 08 (01-May-2022 to 31-May-2022)	N/A
Japan	Takeda Pharmaceutical Company	31-May-2022	Takeda Pharmaceutical Company	31-May-2022
Singapore[a]	N/A	N/A	Novavax Global Sales	N/A
South Korea[a]	https://www.kdca.go.kr/board/board.es?mid=a20501020000&bid=0015&list_no=718699&cg_code=C01&act=view&nPage=1	31-May-2022	SK Bio Distribution Data	31-May-2022
UAE[a]	N/A	N/A	Novavax Global Sales	N/A
UK[a]	Communication from Vaccine Delivery Team Gov.UK/beis	N/A	Novavax Global Sales	N/A

Abbreviations: Refer to List of Abbreviations.
Note: Not Applicable (N/A) indicates source data was unavailable for a given territory or region.
[a] NUVAXOVID
[b] COVOVAX
[c] Cut-off date is not reported by Canada and European Center for Disease Prevention and Control (ECDC). Date presented for Canada and EU in this table is the date of extraction.

Cumulatively, 942,554 NUVAXOVID doses were administered in Australia, Canada, EU, Japan, New Zealand, and South Korea and a total of 46,640,860 NVX-CoV2373 doses (37,432,860 NUVAXOVID and 9,208,000 COVOVAX doses) were distributed globally (Table 2).

Table 2 Cumulative Exposure Data (Distributed and Administered) from Post-Authorisation Experience Presented by Region/LP

Region / LP	Total Doses Administered[a]	Total Doses Distributed[a]
Australia (Biocelect Pty Ltd.)[b]	146,916	6,864,600
Canada (NVX)[b]	5,448	3,238,100
EU (NVX)[b]	258,993	22,479,990
Indonesia (SIIPL)[c]	N/A	9,008,000
Japan (Takeda)[b]	366	1,063,860
New Zealand (Biocelect New Zealand Ltd.)[b]	3,904	1,251,600
Singapore (PharmaEng Technology Pte Ltd)[b]	NA	504,000
South Korea (SK Bioscience)[b]	526,927	2,030,710

Region / LP	Total Doses Administered[a]	Total Doses Distributed[a]
Thailand (SIIPL)[c]	N/A	200,000
NUVAXOVID Total	**942,554**	**37,432,860**
COVOVAX Total	**N/A**	**9,208,000**

Abbreviations: Refer to List of Abbreviations.
Note: Data Sources and cut-off dates are presented in Table 1.
[a] Data presented as recorded.
[b] NUVAXOVID
[c] COVOVAX

5 METHODS

5.1 Search Strategy

5.1.1 Post-Authorization Data

The following search strategy was used to retrieve relevant safety data. A cumulative search of the ARGUS post-authorization safety database was performed with the following Standardised MedDRA Query (SMQ) and High Level Terms (HLTs) with a DLP of 08 Jun 2022:

- SMQ (broad) Noninfectious myocarditis/pericarditis
- HLT Infectious myocarditis
- HLT Infectious pericarditis
- HLT Noninfectious pericarditis
- HLT Noninfectious myocarditis

5.1.2 Clinical Studies

Clinical trial data in the safety analysis set was searched with the SMQ (narrow) Noninfectious myocarditis/pericarditis.

5.2 Analysis Strategy

5.2.1 Adjudication Against a Case Definition

All cases retrieved from post-authorization data were reviewed to assess whether each case met the Brighton Collaboration (BC) case definition of myocarditis and/or pericarditis and which level of diagnostic certainty was applicable.[18]

5.2.2 Causality Assessment

Cases meeting BC case definition Levels 1 – 3 were reviewed at the case level and in aggregate for evidence of causality, including temporal association with NUVAXOVID administration and the presence of any alternative etiologies.

6 RESULTS

6.1 Analysis of Data from Clinical Studies

The data received from clinical studies was assessed with the narrow SMQ: Noninfectious myocarditis/pericarditis. This is a specific search strategy and no adjudication against a case definition was performed on the results of this search strategy.

During the pre-crossover period, two events of myocarditis were reported in the vaccine group and one event was reported in the placebo group (Table 3). During the post-crossover period, two events of pericarditis and one event of myocarditis was reported in the vaccine group and one event of myocarditis was reported in the placebo group (Table 4). The risk difference was not statistically significant during the pre- or post-crossover period.

Table 3 Summary of Unsolicited Adverse Events for Myocarditis or Pericarditis (SMQ) Reported in Pre-crossover Period Safety Analysis Set

	Vaccine	Placebo	Risk Difference
System Organ Class Preferred Term (# of Subjects)	**(n, %, 95% CI) N = 30072**	**(n, %, 95% CI) N = 19877**	**(Vaccine - Placebo) (%, 95% CI)**
Any SMQs	2 (<0.01), (0.00, 0.02)	1 (<0.01), (0.00, 0.03)	0.00 (-0.02, 0.02)
Cardiac disorders	2 (<0.01), (0.00, 0.02)	1 (<0.01), (0.00, 0.03)	0.00 (-0.02, 0.02)
Myocarditis	2 (<0.01)	1 (<0.01)	0.00 (-0.02, 0.02)

Note: Within-group CI is computed using Clopper-Pearson. CI for Risk Difference is based on Miettinen-Nurminen.
SMQ version: 25.0. MedDRA version: 24.0 (2019nCoV-101 Part 1, 2019nCoV-101 Part 2, and 2019nCoV-301), 23.1 (2019nCoV-302), and 23.0 (2019nCoV-501).
Included study data from 2019nCoV-101 Part1 as of 28JUL2021, 2019nCoV-101 Part2 as of 11JUN2021, 2019nCoV-302 as of 27JUL2021, 2019nCoV-501 as of 27OCT2021, and 2019nCoV-301 as of 17FEB2022.
File Name: t_65_3_pre_crossover.rtf. Generated from t_smq_myocarditis_pre_crossover.sas 10MAY2022 16:07

Table 4 Summary of Unsolicited Adverse Events for Myocarditis or Pericarditis (SMQ) Reported in Post-crossover Period

	Vaccine	Placebo	Risk Difference
System Organ Class Preferred Term (# of Subjects)	**(n, %, 95% CI) N = 9635**	**(n, %, 95% CI) N = 18581**	**(Vaccine - Placebo) (%, 95% CI)**
Any SMQs	2 (0.02), (0.00, 0.07)	1 (<0.01), (0.00, 0.03)	0.02 (-0.01, 0.07)
Cardiac disorders	2 (0.02), (0.00, 0.07)	1 (<0.01), (0.00, 0.03)	0.02 (-0.01, 0.07)
Pericarditis	2 (0.02)	0 (0.00)	0.02 (0.00, 0.08)
Myocarditis	1 (0.01)	1 (<0.01)	0.00 (-0.02, 0.05)

Note: Within-group CI is computed using Clopper-Pearson. CI for Risk Difference is based on Miettinen-Nurminen.
SMQ version: 25.0. MedDRA version: 24.0 (2019nCoV-301), 23.1 (2019nCoV-302). Included study data from 2019nCoV-301 as of 17FEB2022, and 2019nCoV-302 as of 27JUL2021.
File Name: t_65_3_post_crossover.rtf. Generated from t_smq_myocarditis_post_crossover.sas 10MAY2022 16:14

6.2 Analysis of Individual Case Safe Reports from Post Authorization Safety Database

6.2.1 Overview of Cases Retrieved

A total of 64 reports were retrieved with the prespecified search strategy. There were 24 events that met Levels 1 – 3 diagnostic certainty for the Brighton Collaboration case definitions for myocarditis and/or pericarditis. Table 5 summarizes the Event Characteristics for reports that met a case definition, Table 6 provides a summary of demographics for all retrieved reports, including those that met a case definition, and Table 7 presents detailed case series information on reports that met the case definitions.

Table 5 Event Characteristics

		Number of Reports	Percentage of Total
Total Reports Retrieved (n)		64	100.0%
Exclusions: Reports Lacking Information to Assess (Case Level 4)		40	62.5%
Total Reports Included in Summary Tables and Case Series		24	37.5%
Country of Incidence (n=24)	Australia	19	79.2%
	Austria	2	8.3%
	Italy	2	8.3%
	Germany	1	4.2%
Serious Cases[a] (n=17)	Fatal	0	0.0%
	Hospitalisation	5	29.4%
	Other	1	5.9%
	IME convention	17	100.0%
MedDRA PT Terms (n=24)[b]	Pericarditis	9	37.5%
	Electrocardiogram abnormal	6	25.0%
	Troponin increased	4	16.7%
	Extrasystoles	3	12.5%
	Echocardiogram abnormal	2	8.3%
	Supraventricular tachycardia	2	8.3%
	Myopericarditis	2	8.3%
	Myocarditis	1	4.2%
	Bundle branch block left	1	4.2%
	Supraventricular extrasystoles	1	4.2%
	Electrocardiogram ST segment abnormal	1	4.2%
	Electrocardiogram change	1	4.2%
	Pericardial effusion	1	4.2%
	Electrocardiogram T wave inversion	1	4.2%

Table 5 Event Characteristics

		Number of Reports	Percentage of Total
Reports Meeting Case Definition (n=24)	Level 2 - Pericarditis	9	37.5%
	Level 3 - Myocarditis	6	25.0%
	Level 2 - Myocarditis	6	25.0%
	Level 3 - Myocarditis Level 3 - Pericarditis	2	8.3%
	Level 1 - Myocarditis Level 2 - Pericarditis	1	4.2%
Event Latency (n=16)	0-7 days	10	62.5%
	8-14 days	5	31.3%
	>15	1	6.3%
Event Treatment[c] (n=5)	Colchicine	3	60.0%
	Ibuprofen	1	20.0%
	Celebrex	1	20.0%
	Beta-blocker therapy and NSAIDs with proton pump inhibitors. 6 months sports ban.	1	20.0%
Event Outcome (as reported in Initial Report) (n=19)	Not Recovered/Not Resolved	14	73.7%
	Recovering/Resolving	4	21.1%
	Recovered/Resolved	1	5.3%

[a] ICSRs may meet more than one seriousness criterion.
[b] Only MedDRA PT terms that pulled the ICSR into the predefined search strategy are listed in this table (See Section 5.1.1). A case may have more than one PT that caused it to be pulled by the search strategy.
[c] Patients may have been treated with more than one type of treatment.

Table 6 Demographics of ICSRs Retrieved

	All Reports (n=64)		Reports Meeting a Case Definition (n=24)	
	Number of Reports	**Percentage of Total Reports**	**Number of Reports**	**Percentage of Total Reports**
Male	**35**	**54.7%**	**14**	**58.3%**
10-19	1	1.6%	1	4.2%
20-29	10	15.6%	2	8.3%
30-39	8	12.5%	4	16.7%
40-49	7	10.9%	5	20.8%
50-59	4	6.3%	1	4.2%
60-69	3	4.7%	0	0.0%
Unknown	1	1.6%	1	4.2%
Female	**29**	**45.3%**	**10**	**41.7%**

Table 6 Demographics of ICSRs Retrieved

	All Reports (n=64)		Reports Meeting a Case Definition (n=24)	
	Number of Reports	**Percentage of Total Reports**	**Number of Reports**	**Percentage of Total Reports**
20-29	7	10.9%	1	4.2%
30-39	5	7.8%	2	8.3%
40-49	7	10.9%	1	4.2%
50-59	3	4.7%	3	12.5%
60-69	4	6.3%	1	4.2%
70-79	2	3.1%	2	8.3%

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
4.1(b)	10-19	Male	3	Pericarditis, Myopericarditis	Level 1 - Myocarditis Level 2 - Pericarditis	Myocarditis: Elevated myocardial biomarker (troponin) Echocardiogram abnormality (wall thickening change) Pericarditis: EKG abnormality (ST segment elevation) Echocardiogram (fluid collection) Cardiac symptom (thoracic tightness)	A 19-year-old male from 4.1(b) with reported medical history of Ventricular septal defect, Seasonal allergy (grasses and pollen), Pyrexia, Heart rate increased, "Electrocardiogram", "Troponin T", and no reported concomitant medications was hospitalized due to medically significant events of Pericarditis and Perimyocarditis three days after receiving Nuvaxovid (unspecified dose). He was noted to have "Non-intervention-required VSD, 3mm / thoracic tightness, subfebrile temperature, and high heart rate up to 130'/min". Diagnostic tests included Echocardiogram (Pericardial thickening up to 8mm in the sense of "adhesion" of the pericardial gap lateral/inferolateral/ inferior, compatible with pericarditis; EF 56%, and only mildly increased pericardial fluid), Electrocardiogram ("normofrequency", sinus rhythm, ST elevations over anterior and posterior wall II, III, aVF, V4-V6); 2nd ECG (at discharge: slight ascending ST changes over anterior wall, discrete horizontal ST elevation aVF and "ECG changes in the sense of (peri-) myocarditis"), and Troponin T (up to 34000 pg/mL). The cardio magnetic resonance imaging was not done. The treatment included beta-blocker therapy, NSAIDs and proton pump inhibitors, and 6 months sports ban. The event was resolving.
4.1(b)	20-29	Male	0	Electrocardiogram, ST segment abnormal, Chest	Level 2 - Pericarditis	Cardiac symptoms (chest pain, dyspnoea)	A 29-year-old male from 4.1(b) with no reported medical history and concomitant medications experienced non-serious events of

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
				discomfort, Chest pain, Dyspnoea		EKG abnormalities (ST elevation)	Chest discomfort, Chest pain, Dyspnoea and Electrocardiogram ST segment abnormal on the same day after receiving Nuvaxovid 10 µg/mL (unspecified dose, 1st dose). Diagnostic tests included Electrocardiogram ('widespread ST elevation'), Echocardiogram (normal) and blood tests (normal). The treatment was unknown, and the outcome of the events was unknown.
4.1(b)	20-29	Male	2	Pericarditis, Chest pain, Dyspnoea, Palpitations, C-reactive protein increased, Electrocardiogram abnormal, Troponin T	Level 2 - Pericarditis	Cardiac symptom (chest pain) EKG abnormality (ST elevation)	A 25-year-old male from 4.1(b) with medical history of allergies and pericarditis following the Pfizer COVID-19 second vaccination dose and concomitant medication of Comirnaty (tozinameran) Covid-19 vaccine experienced a medically significant event of Pericarditis two days after receiving Nuvaxovid (unspecified booster dose) and was admitted for 4-5 hours in the emergency department. Non-serious events of Chest pain, Dyspnoea, Palpitation, C-reactive protein increased, Electrocardiogram abnormal, and Troponin T were also reported. Diagnostic tests included electrocardiogram ("global STE"), Troponin (4), and CRP (33); the result of the chest x-ray was not reported. The treatment included colchicine and ibuprofen. The Pericarditis, Chest pain, Dyspnoea, and Palpitation have not resolved, and the outcome for the rest of the events was unknown.

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
4.1(b)	20-29	Female	UNK	Dysgeusia, Extrasystoles, Palpitations, Headache	Level 3 - Myocarditis	Cardiac symptom (palpitations) Non-specific EKG abnormality (Extrasystoles)	A 23-year-old female from 4.1(b) with no reported medical history and concomitant medications experienced non-serious events of Dysgeusia, Extrasystoles, Headache and Palpitations on an unknown date after receiving Nuvaxovid (unspecified dose). No diagnostic tests were reported. The treatment was unknown, and the outcome of the events was unknown.
4.1(b)	30-39	Male	0	Abdominal pain, Chest discomfort, Chest pain, Flank pain, Electrocardiogram T wave inversion, Dizziness, Arthralgia, Headache, Nausea	Level 3 - Myocarditis	Cardiac symptom (chest pain) Non-specific EKG abnormality (T-wave inversion)	A 35-year-old male from 4.1(b) with medical history of diverticulitis, migraines and right nephrectomy and no concomitant medications experienced medically significant events of Abdominal pain, Arthralgia, Chest discomfort, Chest pain, Electrocardiogram with T wave inversion, Dizziness, Flank pain, Headache and Nausea on the same day after receiving Nuvaxovid (unspecified dose). He presented to the hospital two days later. Diagnostic tests included COVID-19 test (negative), chest x-ray (normal), and Electrocardiogram ("TWI V2, SR"). He was diagnosed with "Chest Pain, unspecified". The treatment was unknown, and the outcome of the events was unknown.
4.1(b)	30-39	Male	8	Arrhythmia, Electrocardiogram abnormal, Chest pain	Level 2 - Myocarditis	Cardiac symptom (chest pain) EKG abnormality: (arrhythmia [Brugada-type ECG])	A 37-year-old male from 4.1(b) with medical history allergy to diphtheria-tetanus vaccine and no reported concomitant medications experienced life-threatening events of Arrhythmia (also medically significant), Electrocardiogram abnormal (Brugada-type ECG) and Chest pain eight days after receiving Nuvaxovid 10ug/mL (dose 0.5 mL). During his

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
							presentation to the hospital his blood pressure was 150/100 mmHg and a "non-brugada syndrome arrhythmia pattern" was detected. The treatment was unknown, and the events have not resolved.
4.1(b)	30-39	Male	11	Chest pain, Electrocardiogram abnormal, Electrocardiogram ST segment elevation, Musculoskeletal chest pain, Pericarditis, Troponin increased	Level 2 - Pericarditis	Cardiac symptom (chest pain) EKG abnormality (ST elevation)	A 30-year-old male from 4.1(b) with no reported medical history and concomitant medications experienced medically significant events of Pericarditis, Chest pain, Electrocardiogram, Electrocardiogram ST segment elevation, Musculoskeletal chest pain, and Troponin 11 days after receiving Nuvaxovid (primary dose 2). Remarkable physical examination findings were "Heart sounds: x2 Murmur", no murmurs, no pericardial rub heard; no tenderness over costochondral joints, but with some tenderness around left midclavicular line. Diagnostic tests included electrocardiogram (Large peaked T waves V3 through V6 with ST elevation in V3 and V4 and ST elevation in lead II and aVF; unlikely ischaemia and much more likely related to pericarditis), Troponin (5). New muscle strain could be a working aetiology as he works on a manual job. The treatment was unknown. The Pericarditis and chest pai have not resolved, and the outcome for the rest events was unknown.
4.1(b)	30-39	Female	14	Tricuspid valve disease, Pericarditis, Chest pain, Dyspnoea, Electrocardiogram	Level 2 - Pericarditis	Cardiac symptom (chest pain, dyspnea) ECG abnormality (ECG reviewed by cardiologist	A 34-year-old female from 4.1(b) with no medical history and concomitant medications experienced medically significant events of Pericarditis and Tricuspid valve disease 14 days after receiving Nuvaxovid (primary dose

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
				abnormal, Arthralgia, Fatigue, Myalgia, Headache		and noted as "probable pericarditis")	1) and presented to the emergency department. Non-serious events of Chest pain, Dyspnoea, Electrocardiogram abnormal, Arthralgia, Fatigue, Myalgia, and Headache were also reported. Diagnostic tests included electrocardiogram ("changes seen by cardiologist and advised probable pericarditis") and echocardiogram ("stable, no myocarditis/pericarditis; mild tricuspid regurgitation only"). The treatment was unknown, and the events have not resolved.
4.1(b)	30-39	Male	62	Chest pain, Troponin Increased	Level 2 - Myocarditis	Cardiac symptom (chest pain Elevated myocardial biomarker (troponin increased [elevated above levels from prior COVID-19 infection])	A 36-year-old male from 4.1(b) with medical history of COVID-19 and no concomitant medications experienced medically significant events of Chest pain and Troponin increased (nadir of 23-25) an unknown date after receiving Nuvaxovid 10 µg/mL (unspecified dose) and presented to the emergency department. Diagnostic tests included Electrocardiogram (normal), and D-dimer (normal). The treatment was unknown, and both events have not resolved.
4.1(b)	30-39	Female	UNK	Supraventricular tachycardia, Chest pain, Dyspnoea, Lethargy	Level 2 – Myocarditis	Cardiac symptoms (dyspnoea, chest pain) EKG abnormality (supraventricular tachycardia)	A 36-year-old female from 4.1(b) with no reported medical history and concomitant medications experienced non-serious events of Chest pain, Dyspnoea, Lethargy and Supraventricular tachycardia on unknown date after receiving Nuvaxovid (unspecified dose, booster dose). No diagnostic tests were reported. The treatment was unknown, and the events have not resolved.

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
4.1(b)	40-49	Male	1	Chest pain, Pericarditis, Electrocardiogram abnormal, Fatigue	Level 2 - Pericarditis	Cardiac symptom (chest pain) EKG Abnormality (cardiologist letter confirms ST elevation)	A 48-year-old fit and healthy male from 4.1(b) with no medical history and concomitant medications experienced medically significant events of Pericarditis, Chest pain, Fatigue and Electrocardiogram abnormal one day after receiving Nuvaxovid (unspecified primary dose) and was hospitalized one day later. Diagnostic tests included Electrocardiogram ("sinus rhythm with some ST elevation consistent with pericarditis"), Echocardiogram (normal), chest x-ray (normal), blood test (mild elevations of the white cell count), and CRP (normal). The treatment included celecoxib and colchicine. The Chest pain, Fatigue and Pericarditis have not resolved and the outcome of the Electrocardiogram abnormal was unknown.
4.1(b)	40-49	Male	5	Pericarditis, Chest discomfort, Chest pain, Dyspnoea, Lymph node pain, Musculoskeletal chest pain, Troponin, Electrocardiogram abnormal	Level 2 - Pericarditis	Cardiac symptoms (chest pain, dyspnoea) EKG abnormality (ST elevation)	A 41-year-old male from 4.1(b) with medical history of asthma and no concomitant medications experienced serious events of Pericarditis, Chest discomfort, Chest pain, and Dyspnoea five days after receiving Nuvaxovid (unspecified dose) and was hospitalized two days later. Non-serious events of Lymph node pain, Musculoskeletal chest pain, Troponin and Electrocardiogram abnormal were also reported. Diagnostic tests included troponin ("6 and 6"), Electrocardiogram ("sinus bradycardia (58 bpm), first degree A-V block and wide-spread ST elevation consistent with early repolarization"), Echocardiogram (mild left atrial dilation, otherwise normal and no pericardial effusion and no Doppler evidence of

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
							constrictive pericardial physiology). The treatment included ibuprofen for 3 days. The Lymph node pain has resolved, pericarditis was resolving and the outcome of the rest of the events was unknown.
4.1(b)	40-49	Female	8	Pericarditis, Pneumonia, Burning sensation, Chest pain, Dyspnoea, Paraesthesia, Tachycardia, Confusional state, Dizziness, Electric shock sensation, Lethargy, Pollakiuria, Echocardiogram abnormal, Tremor, Hypertension, Pain in extremity, Nausea	Level 2 - Pericarditis	Cardiac symptoms (chest pain, dyspnoea) Imaging (evidence of pericardial inflammation by ECHO and CT)	A 45-year-old fit and healthy female from 4.1(b) with no medical history and concomitant medications experienced medically significant events of Pericarditis, Pneumonia, Confusional state and Dizziness, and was hospitalized due to the aforementioned events and with the following events of Burning sensation, Chest pain, Dyspnoea, Electric shock sensation, Hypertension, Lethargy, Nausea, Pain in extremity, Paraesthesia, Pollakiuria and Tachycardia approximately 13 days after receiving Nuvaxovid 10 ug/mL (unspecified dose, first dose). Diagnostic tests included Echocardiogram and CT scan of heart (slight inflammation of pericardium and lung infection), Troponin and blood tests (both "good"); the result of the chest x-ray was not reported. The treatment included Amoxycillin and colchicine. The outcome of the events is unknown.
4.1(b)	40-49	Male	UNK	Myocarditis	Level 3 - Myocarditis	Cardiac symptom (chest pain New EKG abnormality (reduced voltage)	A 47-year-old male from 4.1(b) with no medical history and with concomitant medication of cannabidiol experienced a medically significant event of Myocarditis on an unknown date after receiving Nuvaxovid 10 µg/mL (unspecified dose). He presented with positional chest pain. The physical examination

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
							showed normal heart sounds and no signs of tamponade. Diagnostic tests included Electrocardiogram (' reduced voltage compared to previous'), and chest x-ray (normal). The treatment was unknown, and the event has not resolved.
4.1(b)	40-49	Male	UNK	Asthenia, Dizziness, Extrasystoles, Palpitations, Tachycardia, Fatigue, Nausea	Level 3 - Myocarditis	Cardiac symptom (palpitations) Non-specific symptoms (dizziness, asthenia) Non-specific EKG abnormality (extrasystoles)	A 42-year-old male from 4.1(b) with no reported medical history and reported concomitant medication of Comirnaty experienced non-serious events of Asthenia, Dizziness, Extrasystoles, Palpitations, Tachycardia, Fatigue and Nausea on unknown date after receiving Nuvaxovid (unspecified dose). No diagnostic tests were reported. The treatment was unknown, and the events have not resolved.
4.1(b)	40-49	Male	UNK	Pericardial effusion, Pericarditis, Chest pain, Dizziness, Panic reaction, Troponin	Level 2 - Pericarditis	Cardiac Symptom (chest pain) Imaging (evidence of abnormal fluid collection, which can only be diagnosed thru imaging)	A 42-year-old male from 4.1(b) with no reported medical history and concomitant medications experienced medically significant events of Pericarditis and Pericardial effusion, and non-serious events of Chest pain, Dizziness, Panic reaction and Troponin on unknown date after receiving Nuvaxovid (unspecified dose). No diagnostic tests were reported. The treatment was unknown. The outcome of the Pericarditis, Panic reaction and Troponin was unknown, and the rest of the events have not resolved.
4.1(b)	50-59	Female	0	Respiratory distress, Electrocardiogram change, Joint swelling,	Level 3 - Myocarditis Level 3 - Pericarditis	Cardiac symptom (chest pain) Non-specific EKG abnormality	A 51-year-old female from 4.1(b) with reported medical history of food allergy, fructose intolerance, histamine intolerance, allergy to Dalacin (clindamycin) and Augmentin (amoxicillin / clavulanic acid) and

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
				Dizziness, Chest discomfort, Rash, Pruritus, Arthralgia, Fatigue			oil allergy (perubalsam) and no reported concomitant medications experienced medically significant events of Respiratory distress and Electrocardiogram change on the same day she received Nuvaxovid (unspecified dose). Non-serious events of Joint swelling, Dizziness, Chest discomfort, Rash, Pruritus, Arthralgia and Fatigue were also reported. No diagnostic tests were reported. The treatment was unknown, and the events have not resolved.
4.1(b)	50-59	Female	0	Chest pain, Palpitations, Troponin increased	Level 2 - Myocarditis	Cardiac symptom (chest pain, palpitations) Elevated myocardial biomarker (troponin)	A 50-year-old female from 4.1(b) with medical history of Myocarditis and Pericarditis following the Moderna COVID-19 first vaccination dose and concomitant medication of Moderna Covid-19 vaccine experienced non-serious events of Chest pain, Palpitations and Troponin increased on the same day after receiving Nuvaxovid (unspecified primary dose). Diagnostic tests included Troponin (47). The treatment was unknown, and the events were resolving.
4.1(b)	50-59	Male	3	Pericarditis, Chest Pain, Echocardiogram abnormal	Level 2 - Pericarditis	Cardiac symptom (chest pain) Echocardiogram finding (presumed pericarditis with GP notes imaging findings are consistent/suggestive of pericarditis)	A 58-year-old male from 4.1(b) with no reported medical history and concomitant medications experienced medically significant event of Pericarditis, and non-serious events of Chest pain and Echocardiogram abnormal three days after receiving Nuvaxovid 10 ug/mL (unspecified dose). Diagnostic tests included Echocardiogram ("presumed pericarditis"). The treatment was unknown. The Chest pain has not resolved and the outcome of the Pericarditis and Echocardiogram abnormal was unknown.

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
4.1(b)	50-59	Female	UNK	Supraventricular tachycardia, Asthenia, Chest pain, Dizziness, Dyspnoea, Nausea"	Level 2 - Myocarditis	Cardiac symptoms (chest pain, dyspnoea) Non-specific symptoms (dizziness, asthenia) EKG Abnormality (supraventricular tachycardia)	A 50-year-old female from 4.1(b) with no reported medical history and concomitant medication experienced non-serious events of Supraventricular tachycardia, Asthenia, Chest pain, Dizziness, Dyspnoea and Nausea on unknown date after receiving Nuvaxovid (unspecified primary dose). No diagnostic tests were reported. The treatment was unknown, and the events have not resolved.
4.1(b)	60-69	Female	UNK	Chest pain, Supraventricular extrasystoles, Myalgia	Level 3 - Myocarditis	Cardiac symptom (chest pain) EKG abnormality (supraventricular extrasystoles)	A 69-year-old female from 4.1(b) with no reported medical history and concomitant medication experienced non-serious events of Chest pain, Supraventricular extrasystoles and Myalgia on unknown date after receiving Nuvaxovid (unspecified dose). No diagnostic tests were reported. The treatment was unknown, and the events have not resolved.
4.1(b)	70-79	Female	0	Chest pain, Bundle branch block left, Myalgia, Headache, Pyrexia	Level 3 - Myocarditis Level 3 - Pericarditis	Cardiac symptom (chest pain) Non-specific EKG abnormality (left bundle branch block)	A 72-year-old female from 4.1(b) with reported medical history of respiratory infection and no reported concomitant medications experienced medically significant events of Chest pain, Bundle branch block left and Myalgia on the same day after receiving Nuvaxovid (unspecified primary dose 2), and eight days later, she experienced medically significant events of Headache and Pyrexia. No diagnostic tests were reported. The treatment was unknown. The outcome of the event of Chest pain was resolving; Bundle branch block left has not resolved, and Headache, Myalgia and Pyrexia resolved.

Table 7 Case Series of Adjudicated Cases

Case Number	Age Group (Decade)	Patient Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary
4.1(b)	70-79	Female	UNK	Myopericarditis, Cardiomyopathy, Abdominal pain, Chest pain, Dyspnoea, Electrocardiogram normal, Fibrin D dimer increased, Left ventricular end-diastolic pressure increased, Troponin increased, Urinary tract infection	Level 2 - myocarditis	Cardiac symptoms (chest pain, dyspnoea) Elevated myocardial biomarker (troponin)	A 76-year-old female from 4.1(b) with no reported medical history and reported concomitant medications of Comirnaty (tozinameran) and Astrazeneca Covid-19 vaccines, Aspirin, atorvastatin, hydralazine hydrochloride, mirtazapine, telmisartan, Bisoprolol, and Symbicort experienced medically significant events of Myopericarditis and Cardiomyopathy on unknown date after receiving Nuvaxovid (unspecified primary dose). Non-serious events of Abdominal pain, Chest pain, Dyspnoea, Electrocardiogram normal, Fibrin D dimer increased, Left ventricular end-diastolic pressure increased, Troponin increased and Urinary tract infection were also reported. No diagnostic tests were reported. The treatment was unknown, and the outcome of the events was unknown.
4.1(b)		Male	8	Arrhythmia, Extrasystoles, Axillary pain, Chest pain, Blood pressure increased, Axillary pain, Fatigue	Level 3 - Myocarditis	Cardiac cymptom (chest pain) Non-specific symptom (fatigue) Non-specific EKG abnormality (extrasystoles, arrhythmia)	A male of unknown age from 4.1(b) with no reported medical history and concomitant medications experienced a medically significant event of Arrhythmia eight days after receiving Nuvaxovid (unspecified dose). Non-serious events of Extrasystoles, Axillary pain, Chest pain, Blood pressure increased, Axillary pain and Fatigue were also reported. No diagnostic tests were reported. The treatment was unknown, and the events have not resolved.

7 DISCUSSION AND CONCLUSION

The findings from the clinical data are equivocal. Although a single case is consistent with vaccine induced myocarditis, there is no imbalance across study arms.

Findings in the post authorization setting include an increased number of reports of pericarditis primarily arising from Australia, where active surveillance programs are in place. Signals have not been replicated across regions, nor have they been identified in territories where equivalent exposure has occurred and where emerging safety data is held and analyzed by health authorities (South Korea). While crude observed to expected rates are elevated, it should be noted that the background rates utilized (from the vACCine covid-19 monitoring readinESS [ACCESS] study) were derived prior to the detection of an association of myocarditis with mRNA vaccines, and it is expected that a detection bias exists for observed counts in the current timeframe (i.e., increased sensitivity for the detection of specified adverse events).[19]

Reports meeting a case definition of either pericarditis or myocarditis do not fit the age or gender characteristics of cases arising in association with mRNA vaccines. However, there are consistencies in time to onset. Of 24 reports meeting a case definition at any level, 5 cases involved hospitalizations. There were no fatal events. Where included in reports, treatment of events has been conservative, including treatment with anti-inflammatory drugs. Taken together, these data suggest a causal association with NUVAXOVID but, given the data limitations and, particularly, the absence of signals across geographic regions, a definitive causal association with NUVAXOVID is not confirmed.

8 SAFETY REVIEW TEAM SIGNAL DISPOSITION

The NVX Safety Review Team reviewed the information in this report on 27 Jun 2022. On 05 July 2022, the NVX Safety Review Team considered additional information obtained for generation of NVX monthly SSR #5, database lock of 30 Jun 2022. Notably, cumulative exposure of NUVAXOVID increased from 942,554 to 1,072,074. No new cases meeting a BC Level 1 (definite) definition were reported. Follow-up information was received on a case ([redacted]), previously adjudicated to Level 4, amending the case to Level 2 (probable) and one new Level 3 case was received ([redacted]). Thus, no notable increase in cases was received in the setting of increased exposure, including approximately 40,000 doses in EU.

The NVX Safety Review Team concluded that myocarditis and pericarditis remain important potential risks.

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COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 24-MAY-22 1) 01-JUN-22 2) 09-JUN-22	4.1(b)	Elderly	NUVAXOVID / Injection	UNK: 29-MAR-2022	Bundle branch block left	29-MAR-2022	UNK: 0	Y	Y	Y
		Regulatory Authority	72	1) 1 dosage form Intramuscular	1) -	Not Recovered/Not Resolved					
			Female				0				

Case Narrative

On 08-APR-2022, this initial, serious regulatory authority safety report from 4.1(b) was received from an other health professional via the 4.1(b) (4.1(b)), via the European Medicine Agency 4.1(b) and was received by Novavax on 24-MAY-2022.

A female of 72 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 2 on 29-MAR-2022.

The following medical history was reported: Infection respiratory.
Regulatory Authority patient medical history text: Before in January 22 - completely healthy

No concomitant medications were reported.

On 29-MAR-2022, the day of vaccination, the individual experienced muscle pain (PT: Myalgia) (Serious: Medically Significant), left leg block (PT: Bundle branch block left) (Serious: Medically Significant), and thoracic pain (PT: Chest pain) (Serious: Medically Significant).
On 06-APR-2022, 8 days after vaccination, the individual experienced pyrexia (PT: Pyrexia) (Serious: Medically Significant) and headache (PT: Headache) (Serious: Medically Significant).

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				At the time of reporting, the event outcome of Chest pain was recovering/resolving, Bundle branch block left was not recovered/not resolved, Headache, Myalgia and Pyrexia were recovered/resolved. Lot number was not provided in the report. Regulatory authority's sender comment was provided as follows: The report is for one male patient / one female patient. On 07-JUN-2022, a non-significant case correction based on source document translation was identified. The following information was updated: Event verbatim for PT: Bundle branch block left was updated from "left leg block" to "Left bundle branch block". On 09-JUN-2022, a non-significant case correction was identified. The following information was updated: Follow-up Aware Date and Follow-up PPG Receipt Date was corrected to 01-JUN-2022 from 07-JUN-2022. Institution for secondary reporter was updated to 4.1(b) [redacted] In the narrative, the follow-up statement should have read: On 01-JUN-2022, a non-significant case correction based on source document translation was identified.						
4.1(b) [redacted]	0) 25-MAY-22	4.1(b) [redacted]	Adult	NUVAXOVID / Injection	UNK: 11-MAR-2022	Electrocardiogram change	21-MAR-2022	UNK: 10	Y	Y	Y
		Regulatory Authority	51	1) Intramuscular	1) 4301MF011	Not Recovered/Not Resolved					
			Female				10				
	Case Narrative			On 24-APR-2022, this initial, serious regulatory authority safety report from 4.1(b) [redacted] was received from a consumer via 4.1(b) [redacted] regulatory agency 4.1(b) [redacted]), via the European Medicines Agency (4.1(b) [redacted]) and was received by Novavax on 25-MAY-2022.							

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				A female of 51 years was vaccinated with an unspecified primary dose of intramuscular Nuvaxovid 10 ug/mL on 11-MAR-2022. The following medical history was reported: food allergy, fructose intolerance, histamine intolerance, allergy to Dalacin (clindamycin) and Augmentin (amoxicillin / clavulanic acid) and oil allergy (perubalsam). No concomitant medications were reported. On 11-MAR-2022, after vaccination, the individual experienced joint swelling (PT: Joint swelling), itching (PT: Pruritus), chest pressure (PT: Chest discomfort), rash on arm, neck, face, chest, left foot (PT: Rash), dizziness (PT: Dizziness), thoraxdtuck air problems (PT: Respiratory distress) (Serious: Medically Significant), joint pain (PT: Arthralgia), tiredness (PT: Fatigue), ecg changes (PT: Electrocardiogram change) (Serious: Other medically important condition). At the time of reporting, the event outcomes of Joint swelling, Electrocardiogram change, Rash, Dizziness, Pruritus, Arthralgia, Fatigue, Chest discomfort and Respiratory distress were not recovered/not resolved. The reporters sender comment was as follow: The report is for myself.					
4.1(b)	0) 02-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 21-APR-2022	Tachyarrhythmia	26-APR-2022	1: 5	Y	Y	Y
		Regulatory Authority	64	1) 1 dosage form Intramuscular	1) 4301MF011	Unknown	5				
			Male				5				
Case Narrative			On 23-MAY-2022, this serious initial regulatory authority safety report from 4.1(b) was received from a consumer via the 4.1(b) Regulatory Agency 4.1(b)), via the European Medicines Agency 4.1(b) and was received by Novavax on 02-JUN-2022.								

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				A male of 64 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 21-APR-2022. The following medical history was reported: Comirnaty (tozinameran) (start date: 15-FEB-2022), Hypertension (since 2001), Prostatectomy(in 2013), COVID-19 (Jan-2021), Urinary tract infection (Since 23-APR-2022), Bladder instillation procedure, Limb discomfort, Lithotripsy, Nephrolithiasis, Nocturia and Urinary retention. The following concomitant medications were reported: Daflon 500 mg (diosmin, hesperidin), Levofloxacin 1 A Pharma (levofloxacin) 250 mg (start date: 23-APR-2022), Tamsulosin stada (tamsulosin hydrochloride) 0.4 mg (start date: 2019), Gepan (chondroitin sulfate sodium) (start date: 25-APR-2022), Sevikar 40/5 mg (amlodipine besilate, olmesartan medoxomil), and Pantoprazol 1A Pharma (pantoprazole sodium sesquihydrate) 40 mg. On 21-APR-2022, the individual experienced revaccination with different COVID-19 vaccine (PT: COVID-19 immunisation). On 26-APR-2022, 5 days after vaccination, the individual experienced collapse (PT: Syncope) (Serious: Medically Significant), low blood pressure (PT: Blood pressure decreased) (Serious: Medically Significant), arrhythmia + tachycardia (PT: Tachyarrhythmia) (Serious: Medically Significant), and hemodynamically relevant tachycardia atrial flutters (PT: Atrial flutter) (Serious: Medically Significant). Relevant lab tests included: SARS-CoV-2 test (Result: negative; 25-APR-2022). At the time of reporting, the event outcomes of COVID-19 immunisation, Tachyarrhythmia, Blood pressure decreased, and Syncope were unknown. The event outcome of Atrial flutter was recovered/resolved. No additional information was reported.					
4.1(b)	0) 16-MAR-22 1) 23-MAR-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 23-FEB-2022	Electrocardiogram ST segment abnormal	FEB-2022		N	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	2) 12-APR-22 3) 13-APR-22 4) 17-MAY-22										
		Regulatory Authority	29	1) Intramuscular	1) -	Unknown					
			Male								

Case Narrative

On 01-MAR-2022, this initial, non-serious regulatory authority report from 4.1(b) was received via 4.1(b) reference number: 4.1(b) and was received by Novavax on 16-MAR-2022.

A male of 29 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest discomfort (PT: Chest discomfort), chest pain (PT: Chest pain), dyspnoea (PT: Dyspnoea) and electrocardiogram ST segment abnormal (PT: Electrocardiogram ST segment abnormal).

Relevant lab tests included: Electrocardiogram ST segment (Result: abnormal ; unspecified date).

At the time of reporting, the events outcome of Chest discomfort, Chest pain, Dyspnoea and Electrocardiogram ST segment abnormal were unknown.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

Lot number was not provided in the report.

On 23-MAY-2022, a non-significant case correction was identified. The following information was updated: Electrocardiogram ST segment abnormal was removed from lab data.

On 12-APR-2022, follow-up information was received by Novavax from a health prof in the form of Public Case Details report from 4.1(b) (4.1(b) reference number: 4.1(b)) via 4.1(b)

The 4.1(b) narrative was provided as follows: He had pain and a heavy/tight sensation in the chest from 23/02/2022, starting the day after receiving dose 1 Novavax vaccine against COVID-19. He presented to ED where they report in their letter 'widespread ST elevation' but otherwise normal findings including blood tests. Unfortunately I don't have a copy of this ECG. This is been continuing now for 7 days. He had a flare of symptoms on day 4 and then some slow improvement. He has a heavy sensation in the chest at rest and a worsening of his heaviness/tightness and a recurrence of stabbing pain with light exertion (walking). Follow up blood tests, and echo are WNL, an ECG performed here on 24/02/2022 showed some mild ST changes in leads V2,V3, and lead II, with no associated ST depression in other leads. Medical Hx: Nil significant. The reporter assessed the causality between vaccine and reported events Chest discomfort, Chest pain, Dyspnoea and Electrocardiogram ST segment abnormal as Possible.

No additional information was reported.

On 13-APR-2022, a not significant follow-up information was received by Novavax via 4.1(b) reference number: 4.1(b)) via 4.1(b). The following information was updated in the case: one additional reporter was added to the case.

No additional information was reported.

Based on internal review on 17-MAY-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from "were assessed possible" to "was considered as Possible".

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	The sender comment location was moved from the reporter comment field to the sender comment field.										
4.1(b)	0) 22-MAR-22 1) 24-MAR-22 2) 31-MAR-22 3) 13-APR-22 4) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Myocarditis	01-MAR-2022		Y	Y	Y
		Regulatory Authority	47	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Male								

Case Narrative

On 07-MAR-2022, an initial serious report from 4.1(b) via 4.1(b) (4.1(b) Reference number 4.1(b)) was received by Novavax on 22-MAR-2022.

A male of 47 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

The following concomitant medication was reported: cannabidiol.

On an unspecified date, after vaccination, the individual experienced myocarditis (PT: Myocarditis) (Serious: Medically Significant).

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

At the time of reporting, the event outcome of Myocarditis was unknown.

Lot number was not provided in the report.

On 24-Mar-2022, it was identified that manufacturer control number (MCN) 4.1(b) and 4.1(b) (both assessed as invalid cases) are duplicate to this valid case, 4.1(b) . All source documentation from the invalid cases 4.1(b) and 4.1(b) has been added to this case, 4.1(b) ; however, no significant case-related data was updated in this valid case. This case, 4.1(b) , will be retained; cases 4.1(b) and 4.1(b) remain invalid.
On 24-MAR-2022, a non-significant follow up information was provided. The following information was updated: consumer reporters and social media reporter from invalid cases 4.1(b) and 4.1(b) were added to this valid case 4.1(b) .

On 31-MAR-2022, significant additional information was received by Novavax in the form of Public Case Details report from 4.1(b) reference number- 4.1(b)) via 4.1(b) . The following information has been updated in the case: event onset for myocarditis was updated to 01-MAR-2022; the sender details to 4.1(b) indicates the sender for the follow-up was a Healthcare Professional, hence the event myocarditis was updated to medically confirmed; the outcome of Myocarditis was not recovered/ not resolved/ ongoing; chest X-ray and electrocardiogram were added as lab tests along with their results. The case narrative provided by 4.1(b) is as follows: Presented with positional chest pain and ECG (electrocardiogram) with reduced voltage compared to previous but normal heart sounds and no signs of tamponade. No biochemical or electrical evidence of ischaemia. CXR (chest X-ray) clear.

The Seriousness assessment was assessed by 4.1(as Non-serious.

On 13-APR-2022, non-significant information was received by Novavax via 4.1(b) reference number- 4.1(b)) via 4.1(b) . One additional reporter (4.1(b) delegate) was added to the case. No other additional information was updated in the case.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from 'was assessed as possible' to 'is considered possible'. The sender comment location was moved from the reporter comment field to the sender comment field.									
4.1(b)	0) 22-MAR-22 1) 31-MAR-22 2) 24-MAR-22 3) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 2022	Troponin increased	04-MAR-2022		Y	Y	Y
		Regulatory Authority	36	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Male								

Case Narrative

On 07-MAR-2022, this initial, serious regulatory authority safety report from 4.1(b) was received via 4.1(b) Reference number 4.1(b)) and was received by Novavax on 22-MAR-2022.

A male of 36 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain) and troponin increased (PT: Troponin

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

increased).

At the time of reporting, the event outcomes of Chest pain and Troponin increased were unknown.

Lot number was not provided in the report.

Additional information was received on 31-MAR-2022 in the form of Public Case Details report from 4.1(b)) of a consumer report, via 4.1(b) The case was upgraded to serious based on the new information.
Additional reporters (consumer and 4.1(b) were added to the case. The patient's medical history, laboratory data, suspect product's start date, event onset date for both the events and seriousness criteria of medically significant were updated.
The individual's medical history was updated and included Covid. On an unspecified date in NOV-2021, the patient's troponin was mid to high teens when he was unwell with Covid (captured as Covid 19).
On an unspecified date in 2022, the individual received Nuvaxovid 10 ug/mL.
On 04-Mar-2022, the individual experienced chest pain. On 06-MAR-2022, the individual arrived at the hospital ED (emergency department) (PT: Chest pain) (Serious: Medically significant). Reportedly, the ECG (electrocardiogram) and D-dimer were normal, however, troponin levels were slightly elevated (PT: Troponin increased) (Serious: Medically significant) from previous report in NOV-2021. Reportedly, the new troponin levels were 23-25 (units and normal range unspecified). The individual had no clear answers (unspecified).
The individual was discharged from the hospital and advised to seek GP (general practitioner) and or return to hospital if worsened.
At the time of report, the event chest pain was ongoing and outcome was not recovered/not resolved, and the event outcome of Troponin increased remained unknown.

On 24-Mar-2022, it was identified that manufacturer control number (MCN) 4.1(b) and 4.1(b) (both assessed as invalid cases) are duplicate to this valid case, 4.1(b) . All source documentation from the invalid cases 4.1(b) and 4.1(b) has been added to this case, 4.1(b) ; however, no significant case-related data was updated in this valid case. This case, 4.1(b) will be retained; cases 4.1(b) and 4.1(b) remain invalid.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		On 28-MAR-2022, additional information was received by Novavax from a patient/consumer in the form of Public Case Details report from 4.1(b) reference number: 4.1(b)). The 4.1(b) narrative was provided as follows: Reported chest pain Friday 4th March 2022, ongoing not resolved. Arrived at Hospital ED Sunday 6th March 2022. ECG normal, D-dimer normal, Slightly elevated Troponin levels from previous report in November '21. November troponin when unwell with covid was mid to high teens. New levels are 23-25. Told no clear answer. Discharged and advised to seek GP and or return to hospital if worsens. Hx: Unknown. The reporter assessed the causality of the events as Possible. On 13-APR-2022, additional information in the form of Public Case Details report via 4.1(b) Reference number 4.1(b)) via 4.1(b) , no new information was received. 13-APR-2022, follow-up information was received by Novavax from a business partner in the form of Public Case Details report via 4.1(b) reference number: 4.1(b) via 4.1(b) The 4.1(b) report showed that the event onset date of Troponin increased was updated to 04-MAR-2022 and the event outcome of Troponin increase was not recovered/not resolved.								
4.1(b)	0) 24-MAR-22 1) 12-APR-22 2) 13-APR-22 3) 19-APR-22 4) 21-APR-22 5) 12-APR-22	4.1(b)	Elderly	NUVAXOVID / Injection	UNK: 16-FEB-2022	Supraventricular extrasystoles	23-FEB-2022	UNK: 7	N	Y	Y
		Regulatory	69	1) Intramuscular	1) -	Unknown					

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		Authority									
			Male								
							7				

Case Narrative

On 09-MAR-2022, this initial, non-serious regulatory authority safety report from 4.1(b) was received via 4.1(b) (4.1(b) reference number: 4.1(b)) and was received by Novavax on 24-MAR-2022.

A male of 69 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

The following concomitant medications were reported: Vitamin D3, (colecalciferol), unspecified product (tradename not specified) and St John'S Wort (Hypercum).

On an unspecified date, after vaccination, the individual experienced sinus rhythm (PT: Sinus rhythm) and supraventricular extrasystoles (PT: Supraventricular extrasystoles).

At the time of reporting, the event outcome of Sinus rhythm and Supraventricular extrasystoles was unknown.

Lot number was not provided in the report.

On 12-APR-2022, follow-up information was received by Novavax from a patient/consumer in the form of Public Case Details report via 4.1(b) reference number: 4.1(b)) via 4.1(b).

The Therapeutic Goods Administration narrative was provided as follows: Sinus rhythm, premature atrial contractions, R'R in V1/V2 Refer to the Reaction details.

On 13-APR-2022, follow-up information was received by Novavax in the form of Public Case Details report from the 4.1(b)

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
[redacted]	0) 25-MAR-22 1) 25-MAR-22 2) 25-MAR-22 3) 08-APR-22 4) 13-	[redacted]	Adult	NUVAXOVID / Injection	UNK: 24-FEB-2022	Pericarditis	05-MAR-2022	UNK: 9	Y	Y	Y

[redacted] reference number [redacted]) via [redacted]. On 23-FEB-2022 the individual experienced Sinus rhythm and Supraventricular extrasystoles and the event outcomes for all events were reported as not recovered/not resolved/ongoing.

On 19-APR-2022 a non significant case correction was added as follows: Reporter tab updated. In the narrative tab the sentence from "On 24-MAR-2022 the individual experienced Sinus rhythm and Supraventricular extrasystoles" was changed to On 23-FEB-2022 the individual experienced Sinus rhythm and Supraventricular
extrasystoles. In the On 13-APR-2022, follow-up information was received by Novavax in the for of Public Case Details report from the [redacted] reference number [redacted] via [redacted] ."to "On 13-APR-2022, follow-up information was received by Novavax in the form of Public Case Details report from the [redacted] reference number [redacted]) via [redacted] " In the narrative the causality statement was removed. Remove the paragraph with the information that was updated for the case that was entered after the intro statement for the 12-Apr-22 FUP. Since a narrative was provided in the PCD report, only this narrative should be there for this update. Causality statement was removed after FUP2 since it was not included in the narrative provide by the RA in the PCD report.

On 14-JUN-2022, significant case corrections with Day 0 of 12-APR-2022 was identified. The following information was updated: The reporter details were updated, The Outcome of 'Supraventricular extrasystoles' has been updated to 'Unknown' (Previously reported as not recovered/ not resolved).The sender comment has been moved from the reporter comment field to the Sender comment field. The introductory statement for follow-up narrative from 13-APR-2022 should read as 'On 13-APR-2022, follow-up information was received by Novavax via [redacted] reference number [redacted]) via [redacted] [redacted] received the report on 09-MAR-2022.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	APR-22 5) 17-MAY-22										
		Regulatory Authority	42	1) Intramuscular	1) -	Recovering/Resolving					
			Male				9				

Case Narrative

On 11-MAR-2022, this initial, serious, regulatory authority safety report from [redacted] was received via [redacted] reference number: [redacted] and was received by Novavax on 25-MAR-2022. The initial information was processed with additional information received on 25-Mar-2022 by Novavax via social media monitoring.

A male of 42 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced electrocardiogram (PT: Electrocardiogram) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the events outcome of Electrocardiogram and Pericarditis were unknown.

Lot number was not provided in the report.

On 08-APR-2022, an additional information was received by Novavax from a physician in the form of Public Case Details (PCD) report via [redacted] reference number- [redacted]) via [redacted] Reference number: [redacted]

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				The following information has been updated in the case: Two additional reporters (physician and 4.1(b) were added to the case. The case was medically confirmed upon follow-up. Reportedly, there were no previous vaccine reactions. On 24-FEB-2022, the patient individual was vaccinated with Nuvaxovid. On 05-MAR-2022, 10 days after vaccination, the individual experienced Pericarditis and Electrocardiogram (ECG). On 05-MAR-2022, an ECG was conducted and confirmed Pericarditis. The individual was presented to the hospital emergency department for management of the events. Reportedly, the individual was clinically improving after treatment with celecoxib. The outcome for the event of Pericarditis was recovering/resolving (previously as unknown). No additional information was provided. On 12-APR-2022, a significant case correction with Day 0 of 08-APR-2022 was identified. The following information was updated: The significant follow up aware date was updated from 25-MAR-2022 to 08-APR-2022 but could not be changed on the structured field. An additional non-significant follow up date with day 0 of 25-MAR-2022 was added. The first line of the narrative was updated to include the word safety after regulatory authority and was changed from "received by" to "received via." On 13-APR-2022, follow-up information was received by Novavax from a patient/consumer in the form of Public Case Details report via 4.1(b) 4.1(b) 4.1(b) (4.1(b) reference number: 4.1(b) via 4.1(b) The 4.1(b) report showed the outcome for the event of Electrocardiogram was recovering/resolving. No additional information was reported. Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from assessed as possible to considered possible. The sender comment location was moved from the reporter comment field to the sender comment field.					
4.1(b)	0) 25-MAR-22 1) 12-APR-22 2) 13-APR-22 3) 19-	4.1(b)	Adult	NUVAXOVID / Injection	1: 08-MAR-2022 13:00:00	Electrocardiogram T wave inversion	10-MAR-2022	1: 1.5	Y	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	MAY-22 4) 01-JUN-22										
		Regulatory Authority	35	1) Intramuscular	1) -	Unknown	1.5				
			Male				1.5				

Case Narrative

On 11-MAR-2022, this initial, serious regulatory authority safety report from 4.1(b) was received 4.1(b) 4.1(b) 4.1(b) (4.1(b) reference number: 4.1(b) and was received by Novavax on 25-MAR-2022.

A male of 35 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced abdominal pain (PT: Abdominal pain), arthralgia (PT: Arthralgia), chest discomfort (PT: Chest discomfort), chest pain (PT: Chest pain), electrocardiogram with T wave inversion (PT: Electrocardiogram T wave inversion) (Serious: Medically Significant), dizziness (PT: Dizziness), flank pain (PT: Flank pain), headache (PT: Headache) and nausea (PT: Nausea).

At the time of reporting, the event outcomes of Abdominal pain, Arthralgia, Chest discomfort, Chest pain, Electrocardiogram with T wave inversion, Dizziness, Flank pain, Headache and Nausea were unknown.

Lot number was not provided in the report.

On 12-APR-2022, follow up information was received by Novavax from a patient/consumer in the form of Public Case Details report from

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

4.1(b) 4.1(b) 4.1(b) (4.1(b) reference number: 4.1(b)) via 4.1(b)

The 4.1(b) 4.1(b) 4.1(b) narrative was provided as follows: received first shot of Novavax 1pm Tuesday March 8th. Approx 3 hours later, left abdominal soreness started to flare up - Felt like a flare up of diverticulitis. Later that night March 8th, around bed time started to notice chest tightness - thought it was anxiety - so ignored it and got to sleep. Next day March 9, apart from other symptoms, chest are felt fine until the evening - again thought it was anxiety - so ignored it got to sleep. 3rd day March 10, woke up with tension headache, but with dizziness and nausea. By mid day headache, dizziness and nausea were gone, but chest pain was back more pronounced. Continued all day despite efforts to treat it like anxiety ie (deep breaths, walking etc). That night around midnight, now concerned, rang health line for advice, they advised me to go to the hospital. Spent the early hours of the morning there, was eventually diagnosed with (CHEST PAIN UNSPECIFIED). Chest x-ray clear, Covid Test Clear, ECG: TWI V2, SR. Told it could be muscle soreness around the heart area as part of general muscle soreness and that it hopefully it will clear it self up over the next couple of days. Got home to sleep around 5:30am Woke up 3 hours later to intrusive chest pain sensation. March 11, have had same chest pain all day. Worse laying down. Medical Hx: Migraines, right nephrectomy.

The reporter assessed the causality of the events as possible.

No additional information was reported.

On 14-APR-2022, the following information was updated in the case: all events have the Seriousness criteria of Medically Significant selected.

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from 'assessed as possible' to 'considered possible'.
The sender comment location was moved from the reporter comment field to the sender comment field.

On 01-JUN-2022, non-significant case corrections were identified. The following information was updated:
Reporter's field , additional in formation row # 7, references rows #1 and #4 were updated accordingly.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 29-MAR-22 1) 08-APR-22 2) 08-APR-22 3) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 04-MAR-2022	Pericarditis	04-MAR-2022	UNK: 0	Y	Y	Y
		Regulatory Authority	32	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female				0				

Case Narrative

On 15-MAR-2022, this initial, serious, regulatory authority safety report from 4.1(b) was received via 4.1(b) 4.1(b) 4.1(b) (4.1(b) reference number: 4.1(b) and was received by Novavax on 29-MAR-2022.

A female of 32 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest discomfort (PT: Chest discomfort), chest pain (PT: Chest pain), lethargy (PT: Lethargy) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the events outcome of Pericarditis, Chest discomfort, Chest pain and Lethargy were unknown.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				Lot number was not provided in the report. On 08-APR-2022, additional information was received in the form of Public Case Details report from 4.1(b) reference number: 4.1(b)) via 4.1(b) from a consumer. 4.1(b) narrative was provided as follows: Roughly 30-40 mins after receiving dose, I experienced fairly sharp twinges of pain in my heart. These felt the same as the pain I had on my first and second dose of Pfizer. A week later I still have intermittent twinges of pain and sensation of pressure and burning in my chest. Also feel fatigue and weakness. Reported Reaction: Pericarditis Previous vaccine reactions: No NA Hx: Unknown. The reporter assessed the causality of the events as Possible. On 11-APR-2021, a significant case correction with Day 0 of 08-APR-2021 was identified. The following information was updated: On the patient tab for the historical drug, the reaction PT was coded as chest pain. On the event tab PT: Asthenia and PT: Fatigue were removed, and description as reported for PT: Lethargy was changed from fatigue to Lethargy. On the analysis tab the introductory statement, causality statement of the narrative, and sender comment was updated. On 13-APR-2022, additional information was received in the form of Public Case Details report from 4.1(b) reference number: 4.1(b) via 4.1(b) The following information was updated: The outcome of event Pericarditis was updated from unknown to not recovered/not resolved.						
4.1(b)	0) 29-MAR-22 1) 08-APR-22 2) 12-APR-22 3) 11-APR-22 4) 13-	4.1(b)	Adult	NUVAXOVID / Injection	1: 24-FEB-2022	Pericarditis	01-MAR-2022	1: 5	Y	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	APR-22 5) 17-MAY-22										
		Regulatory Authority	41	1) Intramuscular	1) -	Recovering/Resolving	5				
			Male				5				
	0) 29-MAR-22 1) 08-APR-22 2) 12-APR-22 3) 11-APR-22 4) 13-APR-22 5) 17-MAY-22		Adult	NUVAXOVID / Injection	1: 24-FEB-2022	Electrocardiogram abnormal	04-MAR-2022	1: 8	N	Y	Y
			41	1) Intramuscular	1) -	Unknown	8				
			Male				8				

Case Narrative

On 15-MAR-2022, this serious initial Regulatory Authority Safety Report from 4.1(b) was received by 4.1(b) reference number: 4.1(b)) and was received by Novavax on 29-MAR-2022.

A male of 41 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest discomfort (PT: Chest discomfort), chest pain (PT: Chest pain), dyspnoea (PT: Dyspnoea), troponin (PT: Troponin), lymph node pain (PT: Lymph node pain), musculoskeletal chest pain (PT: Musculoskeletal chest pain), pericarditis (PT: Pericarditis) (Serious: Medically Significant) and electrocardiogram abnormal (PT: Electrocardiogram abnormal).

At the time of reporting, the events outcome of Chest discomfort, Chest pain, Dyspnoea, Electrocardiogram, Lymph node pain, Musculoskeletal chest pain, Pericarditis and Troponin were unknown.

Lot number was not provided in the report.

No further information was provided.

On 08-APR-2022, additional information was received by Novavax in the form of Public Case Details report from 4.1(b) [redacted] reference number 4.1(b) [redacted]) via 4.1(b) [redacted]. The following information was updated in the case: A male of 41 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 24-FEB-2022. The medical history included asthma. The individual was presented to the emergency department on the 03-MAR-2022 at 09:37 hours. As reported, the presenting problem was pain, chest left sided, 2-3 day, Novavax 1/52 (within one week). The individual was seen by the physician and had ECG (Electrocardiogram) performed. At emergency, the individual reported chest tightness and SOB (shortness of breath) worse on exertion affecting usual activities of daily living (ADLS). The pain score was 3/10 ache. The individual was talking in full sentences. The individual's SPO2 (oxygen saturation) was 100, temperature was 35.7 and HR (heart rate) was 46. The diagnosis as reported was cardiovascular chest pain of unknown cause after first vaccine. The individual reported left anterior chest tightness/tenderness (reported as 3 days ago). While trying to surf/sand run, feels worse. The individual went to physician and noted some high ST segments. At ED (emergency department), pain was not pleuritic nor positional, felt mild at rest and had tender chest wall. On examination (OEx), the temperature was 35.7 oxygen saturation was 100 percent, heart rate was 46 and ECG

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

(Electrocardiogram) was reported as 'high takeoff 2, v2, v3, v4, v5, v6, tender chest wall left intncrcostal space rib 6'. The chest was clear with heart sounds dual and nil. Impression: ECG (Electrocardiogram) likely benign early repolarization. The individual underwent serial troponin. Reported as 'traps 6 and 6'. The individual was referred for outpt (outpatient) echocardiogram and advised to take ibuprofen 400mg three times a day for 'the next three days' then cease. The individual was advised the symptoms reflect a chest wall pain and are benign, the echocardiogram would be for added reassurance. Summary of Echogardiogram findings were as followed; the echocardiogram findings include normal LV (left ventricle) systolic function, LVSF70% (normal function 52-70%) with not resting regional wall motion abnormalities. No LV hypertrophy and mild left atrial dilation, no pericardial effusion and no Doppler evidence of constrictive pericardial physiology. The absence of pericardial effusion ir doppler features of constrictive pericardial physiology does not exclude acute pericarditis especially if there are other typical features. Sinus brady cardia with first degree AV block rate 50bpm. The 12 lead ECG performed on "04/03/3033" showed sinus bradycardia, rate 58bpm, first degree A-V block and wide spread ST elevation consistent with early repolarisation and no 12 lead ECG criteria for acute pericarditis. The following information was updated: Onset date for the event Lymph node pain was updated as 28-FEB-2022, and for events chest discomfort, Chest pain, Dyspnoea and Pericarditis was updated as 01-MAR-2022. Onset date for the events Musculoskeletal chest pain and Troponin was updated as 03-MAR-2022, and Electrocardiogram abnormal was updated as 04-MAR-2022. The seriousness, hospitalization, was updated for the events: Chest discomfort, Chest pain, Dyspnoea and Pericarditis. The following laboratory tests were update: Echocardiogram, Electrocardiogram and Nanogram. The event outcome of Lymph node pain was recovered/resolved and the event stop date was 03-MAR-2022. Event outcome of pericarditis was recovering/resolving. The reporter assessed the causality of the events as Possible.

On 12-APR-2022, an additional information was received by Novavax from a consumer in the form of Public Case Details (PCD) report via 4.1(b) reference number 4.1(b) via 4.1(b). The following information has been updated in the case: An additional reporter was added to the case. No additional information was provided.

On 11-APR-2022, non-significant follow-up information was received by Novavax. No new significant information was reported. The following information has been updated:
The 4.1(b) narrative was provided as follows: Lymph nodes sore. Chest sore, shortness of breath, heavy chest, pain in left side when trying to exercise. Chest feels heavy when laying on back. Reported Reaction: Pericarditis Hx:
Asthma Follow up received 16/03/2022 ED Discharge: Pt presented to the Emergency Department on the 3 MAR 2022 at 09:37. The presenting problem was PAIN - CHEST - LEFT

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

SIDED. 2-3 DAYS NOVA VAX 1/52. SEEN BY GP ECG ATTENDED. CHEST TIGHTNESS AND SOB WORSE ON EXERTION AFFECTING USUAL ADLS. PAIN 3/10 ACHE. TALKING IN FULL SENT ACES. SINGLE VAC SP02-T-35.7 SP02-100 HR-46 PMHX-ASTHMA .. The diagnosis was +CARDIO-V ASCULAR - +CHEST PAIN - CHEST PAIN, UNKNOWN CAUSE first vaccine. 3 days ago left anterior chest tightness/tenderness. While trying to surf/sand run, feels worse. Went to GP and noted some high ST segments - ED. pain not pleuritic nor positional. feels mild at rest. tender chest wall. OEx: temp 35.7, sats 1005, HR 46 ECG high takeoff 2, v2, v3, v4, v5, v6 tender chest wall left itncrcostal space Nrib 6. chest is clear, heart sounds dual and nil. impression: ECg likely benign early repolarization. in setting of recent novovax underwent serial tropnonins. traps 6 and 6. in setting recent novovax referred for outpt echocardiogram and advised to take ibuprofen 400mg three times a day for next 3 days then cease. i think your symptoms reflect a chest wall pain and are benign, the echocardiogram would be for added reassurance. Echocardiogram: Summary of findings: The echo findings include normal LV systolic function, LVSF70% (normal function 52-70%) with not resting regional wall motion abnormalities. No LV hypertrophy and mild left atrial dilation, no pericardial effusion and no Doppler evidence of constrictive pericardial physiology. The absence of pericardial effusion ir doppler features of constrictive pericardial physiology does not exclude acute pericarditis especially if there are other typical features. Sinus brady cardia with first degree AV block rate 50bpm. The 12 lead ECG performed on 04/03/3033 showed sinus bradycardia, rate 58bpm, first degree A-V block and wide spread ST elevation consistent with early repolarisation and no 12 lead ECG criteria for acute pericarditis. MPCODECDC

On 13-APR-2022, an additional information was received by Novavax from a consumer in the form of Public Case Details (PCD) report via 4.1(b) reference number 4.1(b)) via 4.1(b) No new information was added to the case.

On 13-APR-2022, additional information was received by Novavax from 4.1(b) reference number 4.1(b) via 4.1(b) . No new information was added to the case.

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from is assessed as possible to were considered possible.
The sender comment location was moved from the reporter comment field to the sender comment field.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 30-MAR-22 1) 08-APR-22 2) 12-APR-22 3) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 22-FEB-2022	Pericarditis	25-FEB-2022	UNK: 3	Y	Y	Y
		Regulatory Authority	58	1) Intramuscular	1) -	Unknown					
			Male				3				
	0) 30-MAR-22 1) 08-APR-22 2) 12-APR-22 3) 13-APR-22		Adult	NUVAXOVID / Injection	UNK: 22-FEB-2022	Echocardiogram abnormal	25-FEB-2022	UNK: 3	N	Y	Y
			58	1) Intramuscular	1) -	Unknown					
			Male				3				

Case Narrative

On 16-MAR-2022, this initial, serious, regulatory authority safety report from 4.1(b) was received by 4.1(b) reference number: 4.1(b)) and was received by Novavax on 30-MAR-2022.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

A male of 58 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain), echocardiogram abnormal (PT: Echocardiogram abnormal) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcomes of Chest pain, Echocardiogram abnormal and Pericarditis were unknown.

Lot number was not provided in the report.

No further information was provided.

Additional information was received on 08-APR-2022 in the form of Public Case Details report from 4.1(b)) via 4.1(b) from a physician. The case became medically confirmed based on the new information.
Additional reporters (physician and 4.1(b) were added to the case. The suspect product's start date, laboratory data, event outcome for the event of chest pain and event onset date for all the events were updated.
The individual's medical history was reported as unknown. Additionally, it was reported that the individual did not have any previous vaccine reactions.
On 22-FEB-2022, the individual received Nuvaxovid 10 ug/mL.
On 25-FEB-2022, three days after the vaccination, the individual experienced chest pain (PT: Chest pain), echocardiogram abnormal (PT: Echocardiogram abnormal) and pericarditis (PT: Pericarditis) (Serious: Medically Significant). Further details included follow-up with GP (general practitioner) and OPD (Outpatient department treatment) echocardiogram presumed pericarditis.
The event of chest pain and echocardiogram abnormal were managed at hospital emergency department (assessed as non-serious by the regulatory authority).

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				At the time of report, the event of Chest pain was not resolved and ongoing, and the event outcome of Echocardiogram abnormal and Pericarditis remained unknown. No additional information was provided. On 12-APR-2022, follow-up information was received by Novavax from a physician in the form of Public Case Details report via 4.1(b) [redacted] reference number 4.1(b) [redacted]) via 4.1(b) . The information received was identical to the previous follow up information received on 08-APR-2022, therefore all the information received was already outlined in the above narrative. However, institution was updated as Regional Pharmacovigilance Centre for primary reporter physician, as this was not added previously. The order in which the reporters show has been altered in the general tab. No other case corrections were made. The Causality has been assessed by 4.1(b) as Possible; the Seriousness assessment was assessed by 4.1(b) as Non-serious. Unspecified modifications were made in the case by 4.1(b) [redacted] on 18-MAR-2022 . The 4.1(b) [redacted] narrative was provided as follows: Chest pain ADDED from Mgt of Event unstructured: Outcome is unknown but ongoing. Further details as provided: GP follow up and OPD echo presumes pericarditis Previous vaccine reactions: No NA Hx: Unknown. No additional information was provided. On 13-APR-2022, follow-up information was received by Novavax from a physician in the form of Public Case Details report via 4.1(b) [redacted] reference number 4.1(b) [redacted]) via 4.1(b) No new information was received.					
4.1(b) [redacted]	0) 31-MAR-22 1) 12-APR-22	4.1(b) [redacted]	Adult	NUVAXOVID / Injection	UNK: 24-FEB-2022	Pericarditis	27-FEB-2022	UNK: 3	Y	Y	Y
		Regulatory Authority	29	1) Intramuscular	1) -	Unknown					

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			Male				3				

Case Narrative

On 17-MAR-2022, a serious, initial, regulatory authority safety report from 4.1(b) was received via 4.1(b) : Reference number 4.1(b) and was received by Novavax on 31-MAR-2022.

A male of 29 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain), dyspnoea (PT: Dyspnoea), nausea (PT: Nausea) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcomes of Chest pain, Dyspnoea, Nausea and Pericarditis were unknown.

Lot number was not provided in the report.

No additional information was provided.

On 12-APR-2022, additional information was received by Novavax from a patient/consumer in the form of Public Case Details report from 4.1(b) reference number: 4.1(b)) via 4.1(b)

The following information was updated in the case: The onset date of vaccination was initially unknown, updated to 24-FEB-2022. The onset date of all events was initially unknown, updated to 27-FEB-2022 for all events. Three reporters were added. The reporter assessed the causality of the events as Possible.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		The 4.1(b) narrative was provided as follows: Central chest pain, sob, nausea Reported Reaction: Pericarditis Previous vaccine reactions: No NA Hx: Unknown									
4.1(b)	0) 01-APR-22 1) 16-APR-22 2) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Extrasystoles	22-FEB-2022		N	Y	Y
		Regulatory Authority	23	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female								

Case Narrative

On 18-MAR-2022, an initial, non-serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b) Reference number 4.1(b) and was received by Novavax on 01-APR-2022.

A female of 23 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced dysgeusia (PT: Dysgeusia), extrasystoles (PT: Extrasystoles), headache (PT: Headache) and palpitations (PT: Palpitations).

At the time of reporting, the event outcomes of Dysgeusia, Extrasystoles, Headache and Palpitations were unknown.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				Lot number was not provided in the report. On 13-APR-2022, follow-up information was received by Novavax in the form of a Public Case Details report from [redacted]; Reference number [redacted]) via [redacted]. At the time of reporting the onset date of the events was 22-FEB-2022 and the outcomes were not recovered/not resolved. On 16-APR-2022, follow-up information was received by Novavax via social media monitoring. No additional information was reported.							
[redacted]	0) 01-APR-22 1) 12-APR-22 2) 13-APR-22 3) 13-APR-22 4) 17-MAY-22	[redacted]	Adult	NUVAXOVID / Injection	2: 16-MAR-2022	Pericarditis	17-MAR-2022	2: 1	Y	Y	Y
		Regulatory Authority	32	1) Intramuscular	1) -	Unknown					
			Male				1				
							1				
Case Narrative				On 18-MAR-2022, this initial serious Regulatory Authority Safety Report from [redacted] was received via [redacted] number [redacted] and was received by Novavax on 01-APR-2022. A male of 32 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date. No medical history was reported.							

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

The following concomitant medications were reported: Spikevax COVID-19 Vaccine (Elasomeran (mRNA)).

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain), chest x-ray normal (PT: Chest X-ray normal) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcomes of Chest pain, Chest X-ray normal and Pericarditis were unknown.

Lot number was not provided in the report.

On 12-APR-2022, additional information was received by Novavax from a physician at a Regional Pharmacovigilance Centre in the form of Public Case Details report from 4.1(b) reference number: 4.1(b) via 4.1(b) . The following information was updated in the case: two additional reporters added including: representative from 4.1(b) and physician at a Regional Pharmacovigilance Centre, updated primary reporter. Updated 4.1(b) reporter to include reporter contact information. Added past medical history of Pericarditis with previous Moderna vaccine and added labs including: chest x-ray and blood tests. Updated Nuvaxovid 10 ug/mL start date to 16-MAR-2022. Updated Spikevax COVID-19 Vaccine (Elasomeran (mRNA)) dose number to 1. Updated onset dates for events of Chest pain, Chest X-ray normal, and Pericarditis to be 17-MAR-2022.

The 4.1(b) narrative was provided as follows: Vaccine given 16/03 presented to ED on AM of 17th with chest pain ADDED from Mgt of Event unstructured: Outcome is unknown but ongoing. Further details as provided: Presented to ED with chest pain. History of Pericarditis with previous Moderna vaccine. Investigated with bloods, CXR - all normal Diagnosis: Pericarditis Previous vaccine reactions: No NA

On 20-APR-2022, a significant case correction with Day 0 of 13-APR-2022 was identified. The following information was updated: Chest pain marked as medically significant.

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			made: The causality was updated from 'assessed to possible to 'is considered possible'. The sender comment location was moved from the reporter comment field to the sender comment field.								
4.1(b)	0) 01-APR-22 1) 12-APR-22 2) 13-APR-22 3) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 15-MAR-2022	Pericarditis	17-MAR-2022	1: 2	Y	Y	Y
		Regulatory Authority	48	1) Intramuscular	1) -	Not Recovered/Not Resolved	2				
			Male				2				
	0) 01-APR-22 1) 12-APR-22 2) 13-APR-22 3) 13-APR-22		Adult	NUVAXOVID / Injection	1: 15-MAR-2022	Electrocardiogram abnormal			Y	Y	Y
			48	1) Intramuscular	1) -	Unknown					
			Male								

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

Case Narrative

On 18-MAR-2022, an initial serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b) Reference number 4.1(b)) and was received by Novavax on 01-APR-2022.

A male of 48 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain), electrocardiogram abnormal (PT: Electrocardiogram abnormal) (Serious: Medically Significant), fatigue (PT: Fatigue) (Serious: Medically Significant) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcomes of Chest pain, Electrocardiogram abnormal, Fatigue and Pericarditis were unknown.

Lot number was not provided in the report.

On 12-APR-2022, additional information was received by Novavax from a patient/consumer in the form of Public Case Details report from 4.1(b); Reference number 4.1(b)) via 4.1(b). The following new information was provided: Medical history was reported as fit and healthy, Dosage information: Dose 1, Administered on 15-MAR-2022, All event onset dates: Chest pain and Fatigue 16-MAR-2022 and Pericarditis 17-MAR-2022 and event outcomes for Chest pain, Fatigue and Pericarditis as Not recovered/not resolved and Unknown for Electrocardiogram abnormal, as well as lab tests: ECG (showed sinus rhythm with some ST elevation consistent with pericarditis), Chest X-ray (normal), Routine bloods (showed a mild elevations of the white cell count), CRP level (normal) and Echocardiogram (normal). The individual was admitted to Private Hospital on 17-MAR-2022 and discharged on 19-MAR-2022 on Celebrex (celecoxib) 200 mg daily and colchicine 500 mcg twice daily.
The reporter assessed the causality of the events as Possible.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

The 4.1(b) narrative was provided as follows:
Received 1st dose of Novavax COVID-19 vaccine. 24 hrs later developed chest pain and heart problem. Emergency admitted to hospital. Still there at time of writing. Reported Reaction: Pericarditis. Medical Hx: Nil allergies, illnesses or previous reactions. Fit and healthy. Follow up received 21/03/2022. Still ongoing pericarditis-chest pain, fatigue Cardiologist letter: Pt was admitted to Private Hospital on the 17th March 2022 with pericarditis. He has enjoyed good health in the past with no health problems. He had received the Novavax Covid-19 vaccine first some 24-36 hours prior to his symptom onset. He presented with pericardial type chest pain, 12 leads ECG's showed sinus rhythm with some ST elevation consistent with pericarditis. A chest Xray was normal. Routine bloods showed a mild elevations of the white cell count. The CRP level was normal. An echocardiogram was normal. His symptoms responded to anti-inflammatory medication in the form of Celebrex and Colchicine. He remained well during a 36 hour observation period and was discharged back to independent living on the 19th March 2022. He was discharged home on Celebrex 200 mg daily, Colchicine 500 mg b.d, he will go onto have a stress echocardiogram as an outpatient.

On 13-APR-2022, additional information was received by Novavax from 4.1(b) reference number: 4.1(b) via 4.1(b) No new information was received.

No additional information was provided.

On 11-MAY-2022, a significant case correction with Day 0 of 13-APR-2022 was identified. The following information was updated: event outcome for Electrocardiogram abnormal was changed from not recovered/ not resolved to unknown.

4.1(b)	0) 01-APR-22 1) 12-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 11-MAR-2022	Pericarditis	13-MAR-2022	1: 2	Y	Y	Y
		Regulatory Authority	48	1) Intramuscular	1) -	Unknown	2				
			Male								
							2				

Case Narrative

On 18-MAR-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b)

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

reference number 4.1(b) and was received by Novavax on 01-APR-2022.

A male of 48 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain), dyspnoea (PT: Dyspnoea), musculoskeletal pain (PT: Musculoskeletal pain), neck pain (PT: Neck pain) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcomes of Chest pain, Dyspnoea, Musculoskeletal pain, Neck pain and Pericarditis were unknown.

Lot number was not provided in the report.

On 12-APR-2022, additional information was received by Novavax from regional pharmacovigilance centre (other healthcare professional) in the form of Public Case details from 4.1(b) reference number: 4.1(b) via 4.1(b) . The following information was updated in the case: Changes for reporter information, dose number along with the date of dosage was included for the vaccine, onset dates for the events were added along with hospitalization information for the appropriate events, and medical confirmation was changed to "Yes."
The 4.1(b) narrative was provided as follows:
Pt has a history of presenting complaints, left side chest pain post Vaccine NOVAVAX. 11am the next day was out in bush, active and sudden intermittent left sided chest pain, rad to left neck and left scapula, accompanied with SOB. the next morning presented to ED, dx with likely pericarditis Previous vaccine reactions: No NA. The reporter assessed the causality of the events as Possible

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
4.1(b)	0) 04-APR-22 1) 12-APR-22 2) 13-APR-22 3) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 24-FEB-2022	Carditis	03-MAR-2022	1: 7	Y	Y	Y
		Regulatory Authority	35	1) Intramuscular	1) -	Not Recovered/Not Resolved	7				
			Female				7				

Case Narrative

On 19-MAR-2022, this serious initial Regulatory Authority Safety Report from 4.1(b) was received via 4.1(b) (Reference number 4.1(b)) and was received by Novavax on 04-APR-2022.

A female of 35 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced carditis (PT: Carditis) (Serious: Medically Significant), chest pain (PT: Chest pain), palpitations (PT: Palpitations), heart rate increased (PT: Heart rate increased), myalgia (PT: Myalgia) and dyspnoea (PT: Dyspnoea).

At the time of reporting, the event outcome of Carditis, Chest pain, Dyspnoea, Heart rate increased, Myalgia and Palpitations were unknown.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
4.1(b)	0) 05-APR-22 1) 05-APR-22 2) 12-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 21-FEB-2022	Myocarditis	25-FEB-2022	1: 4	Y	Y	Y

Lot number was not provided in the report.

No additional information was provided.

On 12-APR-2022, additional information was received by Novavax from a patient/consumer in the form of Public Case Details report from 4.1(b) Reference number: 4.1(b)) via 4.1(b). The following new information was provided:
Dosage information: Dose 1, Vaccine administered 24-FEB-2022, all event onset dates, 03-MAR-2022, and all event outcomes were Not recovered/not resolved/ongoing. Two reporters were added.
The reporter assessed the causality of the events as Possible.

The 4.1(b) narrative was provided as follows: A week after having vaccine. Pains in muscle near collar bone started occurring. As well as elevated heart rate, heart feels inflamed, heart pounding quite hard, pains in chest, and sometimes shortness of breath.

On 13-APR-2022, additional information was received by Novavax from a business partner in the form of Case Line Listing report via 4.1(b) reference number: 4.1(b)) via 4.1(b). No new information was received.

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from 'as assessed as possible' to 'is considered possible'. The sender comment location was moved from the reporter comment field to the sender comment
field.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	3) 13-APR-22 4) 17-MAY-22										
		Regulatory Authority	29	1) Intramuscular	1) -	Not Recovered/Not Resolved	4				
			Female				4				

Case Narrative

On 22-MAR-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b) reference number 4.1(b)) and was received by Novavax on 05-APR-2022.

A female of 29 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain), musculoskeletal chest pain (PT: Musculoskeletal chest pain), myocarditis (PT: Myocarditis) (Serious: Medically Significant) and pain in extremity (PT: Pain in extremity).

At the time of reporting, the event outcomes of Chest pain, Musculoskeletal chest pain, Myocarditis and Pain in extremity were unknown.

Lot number was not provided in the report.

No additional information was provided.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

On 05-APR-2022, follow-up information was received by Novavax from a consumer via social media monitoring. No new information reported.

On 12-APR-2022, additional information was received by Novavax from a Regional Pharmacovigilance Centre in the form of Public Case Details report from 4.1(b) via 4.1(b) . The following information was updated in the case: Additional business partner in the classification tab, two additional reporters(Regional Pharmacovigilance Center and business partner), Date of first vaccination, Event onset dates, Event outcomes.

The reporter assessed the causality of the events as Possible.

On 13-APR-2022, additional information was received by Novavax from a Regional Pharmacovigilance Centre in the form of Public Case Details report from 4.1(b) via 4.1(b) . The following information was updated in the case: Event outcome of Myocarditis, Chest pain and Pain in extremity were updated to Not Recovered/Not Resolved and Onset from Last Dose for all events were updated to 4 days.

The 4.1(b) narrative was provided as follows:

Chest pain, pain in breast bone, pain radiating to the arm Action- went to the GP and cardiologist to run tests necessary to diagnose myocarditis. ADDED from Mgt of Event unstructured: Outcome is known. Further details as provided: The pain subsides. Pain in the breast is not going away Previous vaccine reactions: No NA

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from 'assessed as possible' to 'is considered possible'. The sender comment location was moved from the reporter comment field to the sender comment
field.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 06-APR-22 1) 06-APR-22 2) 12-APR-22 3) 13-APR-22 4) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 02-MAR-2022	Pericarditis	05-MAR-2022	1: 3	Y	Y	Y
		Regulatory Authority	62	1) Intramuscular	1) -	Not Recovered/Not Resolved	3				
			Female				3				

Case Narrative

On 23-MAR-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b) reference number 4.1(b)) and was received by Novavax on 06-APR-2022.

A female of 62 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced, arrhythmia (PT: Arrhythmia) (Serious: Medically Significant), ataxia (PT: Ataxia), axillary lymphadenectomy (PT: Axillary lymphadenectomy), back pain (PT: Back pain), chest pain (PT: Chest pain), chills (PT: Chills), decreased appetite (PT: Decreased appetite), disturbance in attention (PT: Disturbance in attention), dizziness (PT: Dizziness), dysphagia (PT:

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

Dysphagia), dyspnoea (PT: Dyspnoea), eructation (PT: Eructation), hyperhidrosis (PT: Hyperhidrosis), hypoglycaemia (PT: Hypoglycaemia), inflammation (PT: Inflammation), injection site discomfort (PT: Injection site discomfort), lethargy (PT: Lethargy), migraine (PT: Migraine), muscle spasms (PT: Muscle spasms), myalgia (PT: Myalgia), pain (PT: Pain), palpitations (PT: Palpitations), paraesthesia (PT: Paraesthesia), pericarditis (PT: Pericarditis) (Serious: Medically Significant), respiration abnormal (PT: Respiration abnormal) and tremor (PT: Tremor).

At the time of reporting, the event outcomes of Arrhythmia, Ataxia, Axillary lymphadenectomy, Back pain, Chest pain, Chills, Decreased appetite, Disturbance in attention, Dizziness, Dysphagia, Dyspnoea, Eructation, Hyperhidrosis, Hypoglycaemia, Inflammation, Injection site discomfort, Lethargy, Migraine, Muscle spasms, Myalgia, Pain, Palpitations, Paraesthesia, Pericarditis, Respiration abnormal and Tremor were unknown.

Lot number was not provided in the report.

No additional information was provided.

On 06-APR-2022, follow-up information was received by Novavax from a consumer via social media monitoring. No new information was reported.

On 12-APR-2022, additional information was received by Novavax from Consumer in the form of Public Case Details report from 4.1(b) [redacted]. The following information was updated in the case: an additional Classification of Business Partner, three Reporter added, Date of first vaccination (02-MAR-2022), Batch/Lot number was unknown to the reporter, all Event start dates, Event stop dates were added accordingly, and all Event Outcomes were updated. The reporter assessed the causality of the events as Possible and the Serious ICSR as No.

The 4.1(b) [redacted] narrative was provided as follows:
Wednesday March 2nd 2022 1st Novavax vaccination. No reaction at the time or for the following 36 hrs. Felt great. 36 hrs later (Fri 4th): “Normal” (to be expected) muscle aches and lethargy and discomfort around injection site. Sat March 5th those symptoms had dissipated but during the afternoon I got pain in left chest & belching started. Unable to lay flat on my back. Pain less when sitting.4th day after Novavax 72 hours later Sun 6th: Trouble swallowing – choking at times when trying to eat – this continued for about 10 days. Left chest felt swollen heavy and

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

discomfort around heart area. Intermittent sweats Short of breath Very dizzy Tight upper back and neck. Thumping Arrhythmia's intermittently in L chest Extreme lethargy Belching. Unable to lay flat on my back or on left side. Pain less when sitting. Couldn't tolerate bra pressure – for next 2 weeks Hypoglycemic episodes started and continued for 2 days. (Haven't experienced hypoglycaemia for 9 months). Muscle cramps not just aches. 5th day after Novavax (Mon 7th). Pain increased in T6 area in back (where I had a fracture last year) and through the upper spine/neck felt very inflamed. Intermittent piercing pain in left chest continued until day 10. Dizzy Belching Lymph gland slightly tender in left armpit. (Only for 1 day). 8th day after immunisation (Thursday 10th). Pain when lifting arms above chest height – e.g. at clothesline or to wash hair. Diagnosed with Pericarditis by Cardiologist and began Colchicine medication. Agghh!!! Pericarditis for the 3rd time in 9 months!! Last year I felt 12/10 pain for several months while having Pericarditis but this time it has been a manageable 6/10 pain down to 2/10 now. 10th & 11th day after Novavax immunisation: (Sat 12th and Sun 13th) Pain subsiding. But still need to rest numerous times during day. 12th day after Novavax (Mon 14th) Woke with zest! But needed to rest 2 times during day. Pain in T6 area and upper back after lifting arms. 13th day after Novavax (Tues 15th) Woke 4am with entire torso feeling inflamed internally and upper back. Couldn't tolerate bra pressure. Reaching above chest induced back pain and slight breathing discomfort. Bed rest 4 x during day.15th day after Novavax (Thurs 17th) Felt great. Did not need the usual 2 or 3 sleeps during the day. However muscle pain in left neck and left upper back continued intermittingly for days following and still needed to rest and overcome shortness of breath any time after attempting any physical task. 3 weeks after Novavax immunisation: All chest symptoms dizziness & extreme lethargy non-existent. Intense muscle aches non-existent but have ongoing muscle stiffness and pain and a feeling of some inflammation in upper back-neck-shoulders. Requiring massage several times a day for comfort and mobility. Still unable to lay on left side without inducing pain in left ribs/chest and heavy feeling in chest when sleeping. Alleviated by not laying on side. Still can't tolerate bra pressure after an hour or so. Belching continues. Advised by Cardiologist to continue Colchicine for 3 months and not to have 2nd Novavax on 23rd March as scheduled having had Pericarditis three times and Pleurisy once in the last 9 months; then reassess suitability for next vaccination after 3 months. COVID Team - As above and per the same information as attached by client. - Client requested an exemption and process was advised. Reported Reaction: Loss of appetite Chills Myalgia Paresthesia Ataxia Lethargy Palpitations Tremor Migraine Dysphagia Altered breathing Hypoglycemia Pericaditis Mental capacity reduced Wednesday March 2nd 2022 1st Novavax vaccination. No reaction at th Other vaccines in the last 4 weeks: N Allergies: Y Illness at the time of vaccination: N Hx: Numerous relating to Brugada and numerous other food and drug allergies. A list is available from me by request and was provided at the time of vaccination. COVID TEAM PmHx - Numerous relating to Brugada and numerous other food and drug allergies. A list is available from me by request and was provided at the time of vaccination. COVID TEAM PmHx - Brugada Pericarditis hyperinsulinemia. Client is to email a list of food and drug allergies. Client is to email a list of food and drug allergies.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		On 13-APR-2022, additional, multiple follow-up information was received by Novavax via 4.1(b) reference number: 4.1(b) via 4.1(b) including a line listing. No significant information was reported in the source documents. The onset date was stated as 04-MAR-2022 for all PTs in the line listing which appears broadly consistent with the various dates presented in the Public case details. No additional information was provided.									
4.1(b)	0) 06-APR-22 1) 12-APR-22 2) 13-APR-22 3) 13-APR-22 4) 17-MAY-22 5) 25-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	1: MAR-2022	Pericarditis	03-MAR-2022		Y	Y	Y
		Regulatory Authority	28	1) Intramuscular	1) -	Unknown					
			Male								
Case Narrative		On 23-MAR-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b) reference number 4.1(b)) and was received by Novavax on 06-APR-2022. A male of 28 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date. No medical history was reported.									

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest pain (PT: Chest pain) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcomes of Chest pain and Pericarditis were unknown.

Lot number was not provided in the report.

No additional information was provided.

On 12-APR-2022, additional information was received by Novavax from regional pharmacovigilance center (other healthcare professional) in the form of Public Case details from 4.1(b) reference number: 4.1(b)) via 4.1(b) .

The reporter assessed the causality of the events pericarditis and chest pain as Possible.

The 4.1(b) narrative was provided as follows:

A Male patient exhibited the following symptom(s) for the duration(s) noted: see below from 03/03/2022; Chest pain for 3 nights; worse when lying down. Patient was managed by Hospital emergency department. Check at Hospital; under cardiology - diagnosed with Pericarditis; had bloods; CXR; ECG; ECHO; discharged home with Colchicine. Cardio f/u in 8 weeks; no date yet; Needs advise - regarding his 2nd dose; ? can he have this or needs alternative - ? if so; which one and what is the schedule. Patient medical history includes Nil;allergies: codein-urticaria; at the time of vaccination patient was not ill. This AEFI was sent to the Vaccine Clinical Triage Group for review.

On 13-APR-2022, additional information in the form of Public Case Details report via 4.1(b) Reference Number 4.1(b)) via 4.1(b) , No new information was received.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				On 19-APR-2022, a significant case correction with Day 0 of 13-APR-2022 was identified. The following changes were made: case narrative was changed reflecting RA case narrative, new reporter from 4.1(b) was added, non-significant FU row for follow-up 2. Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from 'were assessed as possible' to 'is considered possible'. The sender comment location was moved from the reporter comment field to the sender comment field. On 25-MAY-2022, a non-significant case correction was identified. The following information was updated: In sender comment, Pericarditis statement was updated to: "The event Pericarditis was assessed as serious" (previously written as 'reported as serious').							
4.1(b)	0) 07-APR-22 1) 12-APR-22 2) 21-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 24-FEB-2022	Pericarditis	FEB-2022		Y	Y	Y
		Regulatory Authority	Unknown	1) Intramuscular	1) -	Unknown					
			Male								

Case Narrative

On 24-MAR-2022, an initial serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b); Reference number 4.1(b) and was received by Novavax on 07-APR-2022.

A male of 29 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced abdominal pain (PT: Abdominal pain), arthralgia (PT: Arthralgia), headache (PT: Headache), lethargy (PT: Lethargy), myalgia (PT: Myalgia), pericarditis (PT: Pericarditis) (Serious: Medically Significant) and pyrexia (PT: Pyrexia).

At the time of reporting, the events outcome of Abdominal pain, Arthralgia, Headache, Lethargy, Myalgia, Pericarditis and Pyrexia were unknown.

Lot number was not provided in the report.

No additional information was provided.

On 12-APR-2022, additional information was received by Novavax from a regional pharmacovigilance centre in the form of Public Case Details report from 4.1(b) reference number 4.1(b)) via 4.1(b) . The following information was updated in the case: updated onset dates for events, added 4.1(b) reporter and business partner within classification section.

The 4.1(b) narrative was provided as follows:
Fever 37.7; Chills; Headache; Muscle/body aches; Joint aches/pain; Nausea; Abdominal pain; Fatigue/tiredness; Pericarditis. ADDED from Mgt of Event unstructured: Outcome is unknown but ongoing. Further details as provided: Ongoing symptoms, Days missed from work etc: 2 days. Previous vaccine reactions: No NA Hx: Unknown

On 21-APR-2022, additional information was received by Novavax from a consumer in the form of Public Case Details report from 4.1(b) reference number: 4.1(b)) via 4.1(b) No new information was received.The 4.1(b) narrative was provided as follows:
Fever 37.7; Chills; Headache; Muscle/body aches; Joint aches/pain; Nausea; Abdominal pain; Fatigue/tiredness; Pericarditis. ADDED from Mgt of Event unstructured: Outcome is unknown but ongoing. Further details as provided: Ongoing symptoms, Days missed from work etc: 2 days.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		Previous vaccine reactions: No NA Hx: Unknown.									
4.1(b)	0) 08-APR-22 1) 08-APR-22 2) 13-APR-22 3) 17-MAY-22 4) 04-MAY-22 5) 25-APR-22 6) 03-MAY-22 7) 03-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 17-FEB-2022	Pericarditis	17-FEB-2022	UNK: 0	Y	Y	Y
		Regulatory Authority	23	1) Intramuscular	1) -	Unknown					
			Male				0				
	0) 08-APR-22 1) 08-APR-22 2) 13-APR-22		Adult	NUVAXOVID / Injection	UNK: 17-FEB-2022	Echocardiogram abnormal	17-FEB-2022	UNK: 0	N	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	3) 17-MAY-22 4) 04-MAY-22 5) 25-APR-22 6) 03-MAY-22 7) 03-MAY-22										
			23	1) Intramuscular	1) -	Unknown					
			Male								
							0				

Case Narrative

On 25-MAR-2022, an initial serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b); Reference number 4.1(b) and was received by Novavax on 08-APR-2022.

A male of 23 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced blood bilirubin increased (PT: Blood bilirubin increased), chest discomfort (PT: Chest discomfort), chest pain (PT: Chest pain), dizziness (PT: Dizziness), echocardiogram abnormal (PT: Echocardiogram abnormal), malaise (PT: Malaise), mitral valve thickening (PT: Mitral valve thickening) (Serious: Medically Significant), palpitations (PT: Palpitations), pericarditis (PT: Pericarditis) (Serious: Medically Significant) and tachycardia (PT: Tachycardia).

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

At the time of reporting, the events outcome of Blood bilirubin increased, Chest discomfort, Chest pain, Dizziness, Echocardiogram abnormal, Malaise, Mitral valve thickening, Palpitations, Pericarditis and Tachycardia were unknown.

Lot number was not provided in the report.

No additional information was reported.

On 08-APR-2022, additional information was received by Novavax via social media monitoring. No new information was added to the case.

On 13-APR-2022, follow-up information was received by Novavax from a patient/consumer in the form of Public Case Details report via 4.1(b) reference number: 4.1(b)) via 4.1(b) . The following information was updated in the case: One additional reporter was added to the case. The date of vaccination added as FEB-2022. Onset dates added for all events as 17-FEB-2022. Seriousness criteria: Hospitalization selected for events Blood bilirubin increased, Chest discomfort, Chest pain, Dizziness, Malaise, Mitral valve thickening and Palpitations and Medically significant selected for events Electrocardiogram abnormal and Tachycardia. Echocardiogram (Result: with abnormal results, 50% prolapse with significant thickening of the mitral valve leaflet tip, mild to moderate regurgitation; Date: 17-FEB-2022), DNA Antibody (Result: 705-175 on anti-DNA-sb-blood test; Date: unspecified),Liver function test (Result: 55 bilirubin levels; Date: unspecified) and Blood test (Result: indicated recent infection/bug) added as lab tests. Historical condition (PT: Asthma) was added to the patient tab. Outcome of events: Chest discomfort, Chest pain, Dizziness, Malaise, Palpitations and Tachycardia changed to not recovered/not resolved.

The causality between the vaccine and reported events: Blood bilirubin increased, Chest discomfort, Chest pain, Dizziness, Echocardiogram abnormal, Malaise, Mitral valve thickening, Palpitations, Pericarditis and Tachycardia were assessed as possible.

The 4.1(b) narrative was provided as follows: No treatments as such, Echocardiogram with abnormal results, 50% prolapse with significant thickening of the mitral valve leaflet tip, mild to moderate regurgitation , 705-175 on a anti-DNA-sb blood test, 55 bilirubin levels for my liver, Never have I ever had levels so high, The blood test indicates I've had a recent infection/bug, I know for a fact it came from the vaccine because I never had any symptoms or problems until I had the vaccine, and it was suddenly Reported Reaction: Palpitations with chest pain and a abnormal echocardiogram results, dissyness cold sensation in my heart area once within 5 minutes of receiving the vaccine, rapid

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

heartbeat, strong heartbeat, general sense of feeling unwell Hx: Asthma.

On 04-MAY-2022, it was identified that manufacturer control number (MCN) 4.1(b) is a duplicate to this case 4.1(b) . The information from case 4.1(b) has been added to this case, 4.1(b) . This case, 4.1(b) will be retained and this case 4.1(b) will be invalidated.

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from 'were assessed as possible' to ' considered possible'. The sender comment location was moved from the reporter comment field to the sender comment field.

On 10-JUN-2022, significant case corrections were identified. The following follow up statements should have been added to the narrative: On 11-APR-2022, a follow up regulatory authority safety report was received from a consumer via 4.1(b) reference number: 4.1(b) in the form of Public Case Details (PCD) report via 4.1(b) and received by Novavax on 20-Apr-2022. On 25-APR-2022, additional information was received by Novavax in the form of Public Case Details (PCD) report from 4.1(b) reference number 4.1(b) and added to the subordinate case. Individual's age was updated to 23 years old. On 03-MAY-2022 4.1(b) was identified to be a subordinate duplicate case of 4.1(b) and not on 04-MAY-2022 as previously stated. Two additional events Heart valve incompetence and Infection were added with start date of 17-Feb-2022, Outcome: Unknown. Unchecked medically significant for events Tachycardia and Echocardiogram abnormal. Updated hospitalization details for all the serious events. Updated lab date and product administration date. Added all the source documents from the subordinate case to this master case. Added the reference number. Corrected the spelling and grammar mistakes.

A conflict within the reports was also identified: In the source document from the 4.1(b) received on 13-APR-2022, the patient age was reported as 23. In the source document from the 4.1(b) received on 04-MAY-2022, the patient age was reported as 24. It was unclear whether the age provided in each source document was given as the age at event onset, or the age at case retrieval.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 11-APR-22 1) 13-APR-22 2) 13-APR-22 3) 21-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 25-MAR-2022	Pericarditis			Y	Y	Y
		Regulatory Authority	27	1) Intramuscular	1) -	Unknown					
			Male								

Case Narrative

On 28-MAR-2022, this initial serious Regulatory Authority Safety Report from 4.1(b) was received via 4.1(b) (Reference number: 4.1(b)) and was received by Novavax on 11-APR-2022.

A male of 28 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

On an unspecified date, the individual also received a co-suspect Comirnaty (tozinameran) COVID-19 vaccine at an unknown dose.

The individual reported an unspecified current medical condition.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced concomitant disease aggravated (PT: Concomitant disease aggravated), dizziness (PT: Dizziness) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the events outcome of Pericarditis, Concomitant disease aggravated and Dizziness were unknown.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				Lot number was not provided in the report. On 13-APR-2022, follow-up information was received by Novavax from other health professional in the form of Public Case Details report from 4.1(b) reference number: 4.1(b)) via 4.1(b) The 4.1(b) narrative was provided as follows: Client has an extensive medical history along with allergies - non of which were contraindicated to receive Novavax (received Pfizer for his first two doses and developed pericarditis hence received novovax as his booster). Whilst in the observation area he developed dizziness and was taken to lie down, whilst there he further developed symptoms consistent with his known medical condition of hemiplegia migraines, which he requires medication to control, none of which we stocked at the hub (aspirin). It was decided he was stable enough to leave the hub in the company of his mum to go home and get the relevant medication however he ended up going to ED upon discussion with his mum as he requires IV largactil. Given he has had side effects (whether the symptoms post his novavax reaction are related are elated to vaccine is unknown) and Pfizer, I fell follow up would be warranted and appreciated by his mother! Previous vaccine reactions: No NA Hx: Unknown. The causality between vaccine and reported events: Concomitant disease aggravated, Dizziness and Pericarditis were reported as possible. On 21-APR-2022, a non-significant case correction was identified. The following information was updated: Dose number '1' was removed for suspect products NUVAXOVID and COMIRNATY from the product tab.						
4.1(b)	0) 11-APR-22 1) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 01-MAR-2022	Pericarditis	MAR-2022		Y	Y	Y
		Regulatory Authority	28	1) Intramuscular	1) -	Unknown					
			Female								
Case Narrative				On 28-MAR-2022, this initial serious Regulatory Authority Safety Report from 4.1(b) was received via 4.1(b) (Reference number: 4.1(b)) and was received by Novavax on 11-APR-2022.							

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

A female of 27 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcome of Pericarditis was unknown.

Lot number was not provided in the report.

No additional information was provided.

On 13-APR-2022, additional information was received by Novavax from a Regional Pharmacovigilance Centre in the form of Public Case Details (PCD) report from 4.1(b) reference number 4.1(b) via 4.1(b)

The following information had been updated in the case: Age of the individual was updated to 28 years. Onset dates of the event pericarditis was updated as MAR-2022 and the event outcome was updated as unknown. Treatment start date was provided as 01-MAR-2022. Lab data was updated.

The reporter assessed the causality between vaccine and reported events as possible.

The 4.1(b) narrative was provided as follows:
GP referral to immunology attached* ECG confirmed Pericarditis Ethnic sub group unstructured: Unknown Previous vaccine reactions: No NA Hx: Unknown.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		On 13-APR-2022, additional information was received by Novavax from a business partner in the form of Case Line Listing report from [redacted] reference number: [redacted]) via [redacted].									
[redacted]	0) 11-APR-22 1) 13-APR-22 2) 13-APR-22 3) 17-MAY-22 4) 31-MAY-22	[redacted]	Adult	NUVAXOVID / Injection	1: MAR-2022	Pericarditis	14-MAR-2022		Y	Y	Y
		Regulatory Authority	45	1) Intramuscular	1) -	Unknown					
			Female								
	0) 11-APR-22 1) 13-APR-22 2) 13-APR-22 3) 17-MAY-22 4) 31-MAY-22		Adult	NUVAXOVID / Injection	1: MAR-2022	Echocardiogram abnormal			Y	Y	Y

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			45	1) Intramuscular	1) -	Unknown					
			Female								

Case Narrative

On 11-APR-2022, this initial, serious regulatory authority safety report from 4.1(b) was received via 4.1(b) (Reference number: 4.1(b)) and was received by Novavax on 11-APR-2022.

A female of 45 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced burning sensation (PT: Burning sensation), chest pain (PT: Chest pain), confusional state (PT: Confusional state), dizziness (PT: Dizziness), dyspnoea (PT: Dyspnoea), electric shock sensation (PT: Electric shock sensation), hypertension (PT: Hypertension), lethargy (PT: Lethargy), nausea (PT: Nausea), pain in extremity (PT: Pain in extremity), paraesthesia (PT: Paraesthesia), pericarditis (PT: Pericarditis) (Serious: Medically Significant), pneumonia (PT: Pneumonia) (Serious: Medically Significant), pollakiuria (PT: Pollakiuria) and tachycardia (PT: Tachycardia).

At the time of reporting, the events outcome of Burning sensation, Chest pain, Confusional state, Dizziness, Dyspnoea, Electric shock sensation, Hypertension, Lethargy, Nausea, Pain in extremity, Paraesthesia, Pericarditis, Pneumonia, Pollakiuria and Tachycardia were unknown.

Lot number was not provided in the report.

No additional information was provided.

On 27-MAR-2022, follow up information was received from a patient/consumer by Novavax in the form of Public Case Details report from 4.1(b) reference number : 4.1(b)) via 4.1(b) on 13-APR-2022.The 4.1(b)

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

narrative was provided as follows:
Young 45 year old female, very fit and healthy, no underlying health conditions Dizziness and burning head 30 minutes after first injection of Nuvaxovid. 5 days post injection: burning sensation of the head, electric feeling in limbs, dizziness, nausea, lethargy, brain fog. 6 days post injection: tingling feeling of arms and legs, lethargy, burning sensation of head, trembling and shaking. No fever. 8 days post injection: 3am chest pains, tachycardia, high blood pressure, shaking, trembling, electric shock feeling in limbs, shortness of breath, dizziness, brain fog, burning sensation of head and neck. Called Ambulance, admitted to Emergency department at hospital. Had CT scans of lungs and heart, XRay of chest , blood works. Admitted to Cardiology Ward for further tests. Had further CT scan of heart, Echocardiogram of heart. Results show slight inflamation of pericardium and lung infection. Troponin levels good, blood works good. Discharged 3 days later on Amoxycillin antibiotics and Colchicine for pericarditis. For further cardiology review in 6 weeks. Awaiting Hospital Discharge Summary letter from Hospital. Hx: None.

At the time of reporting 29-MAR-2022, the event outcome of Burning sensation was not recovered/not resolved, Chest pain was not recovered/not resolved, Confusional state was not recovered/not resolved, Dizziness was not recovered/not resolved, Dyspnoea was not recovered/not resolved, Electric shock sensation was unknown, Hypertension was not recovered/not resolved, Lethargy was not recovered/not resolved, Nausea was unknown, Pain in extremity was not recovered/not resolved, Paraesthesia was not recovered/not resolved, Pericarditis was unknown, Pneumonia was unknown, Pollakiuria was not recovered/not resolved and Tachycardia was not recovered/not resolved.

Based on internal review on 17-MAY-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from 'assessed as possible' to 'considered as possible'.
The sender comment location was moved from the reporter comment field to the sender comment field.

On 31-MAY-2022, it was identified that manufacturer control number (MCN) 4.1(b) , is a duplicate to this case, 4.1(b) . The information from 4.1(b) has been added to this case, 4.1(b) . This case, 4.1(b) will be retained and 4.1(b) will be invalidated.
The following information was added to this case: Two additional serious events of Echocardiogram abnormal (PT: Echocardiogram abnormal) (Serious: Medically Significant) and Tremor (PT: Tremor) (Serious: Medically Significant) were added.
The 4.1(b) narrative was provided as follows: A female patient exhibited the following symptom(s) for the duration(s)

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country / Source	Patient Age Group / Age / Sex	Product Name / Formulation / Dose Details - All	Dose number: Dose Start Date / Batch Numbers	Event Preferred Term / Event Outcome	Event Onset Date / Time To Onset-First dose / Time To Onset-Second Dose / Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				noted: Young 45 year old female; very fit and healthy; no underlying conditions Dizziness and burning head 30 minutes after first injection of Nuvaxovid. 5 days post injection: burning sensation of the head; electric feeling in limbs; dizziness; nausea; lethargy; brain fog. 6 days post injection: tingling feeling of arms and legs; burning sensation of head; trembling and shaking. No fever. 8 days post injection: 3am chest pains; tachycardia; high blood pressure; shaking; trembling; electric shock feeling in limbs; shortness of breath; dizziness; brain fog; burning sensation of head and neck. Called Ambulance; admitted to Emergency department at hospital. Had CT scans of lungs and heart; Xray of chest; blood works. Admitted to Cardiology Ward for further tests. Had further CT can of heart; Echocardiogram of heart. Results show slight inflammation of pericardium and lung infection. Troponin levels good; blood works good. Discharged 3 days later on Amoxycillin antibiotics and Colchicine for pericarditis. For further cardiology review in 6 weeks. Awaiting Hospital Discharge Summary letter from Hospital. Hx: None. Patient was managed by Hospital admission. Hospital. Patient medical history includes at the time of vaccination patient was not ill. This AEFI was sent to the Vaccine Clinical Triage Group for review.						
4.1(b)	0) 13-APR-22 1) 13-APR-22 2) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Pericarditis	24-MAR-2022		Y	Y	Y
		Regulatory Authority	41 Female	1) Intramuscular	1) -	Not Recovered/Not Resolved					
	0) 13-APR-22 1) 13-APR-22 2) 17-MAY-22		Adult	NUVAXOVID / Injection	UNK: UNK	Electrocardiogram abnormal	24-MAR-2022		N	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			41	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female								

Case Narrative

On 30-MAR-2022, an initial serious Regulatory Authority safety report from 4.1(b) was received via 4.1(b) ; Reference number 4.1(b) and was received by Novavax on 13-APR-2022.

A female of 41 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On an unspecified date, after vaccination, the individual experienced chest discomfort (PT: Chest discomfort), chest pain (PT: Chest pain), dyspepsia (PT: Dyspepsia), electrocardiogram abnormal (PT: Electrocardiogram abnormal), hypertension (PT: Hypertension), palpitations (PT: Palpitations) and pericarditis (PT: Pericarditis) (Serious: Medically Significant).

At the time of reporting, the event outcomes of Chest discomfort, Chest pain, Dyspepsia, Electrocardiogram abnormal, Hypertension, Palpitations and Pericarditis were unknown.

Lot number was not provided in the report.

No additional information was provided.

On 13-APR-2022, follow-up information was received by Novavax from 4.1(b) reference number: 4.1(b)) via 4.1(b) . Outcome of the events Chest discomfort, Chest pain, Dyspepsia, Electrocardiogram abnormal, Hypertension, Palpitations and

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				Pericarditis was provided as Not recovered/Not resolved and the onset date for events Chest discomfort, Chest pain, Dyspepsia, Electrocardiogram abnormal, Hypertension, Palpitations and Pericarditis was updated to 24-MAR-2022. No additional information was reported. Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from 'assessed as possible' to 'considered as possible'. The sender comment location was moved from the reporter comment field to the sender comment field.						
4.1(b)	0) 13-APR-22 1) 13-APR-22 2) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Pericarditis	15-MAR-2022		Y	Y	Y
		Regulatory Authority	23	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Male								

Case Narrative

On 30-MAR-2022, this serious, initial, Regulatory Authority safety report from 4.1(b) was received via 4.1(b) reference number: 4.1(b) and was received by Novavax on 13-APR-2022.

A male of 23 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				On an unspecified date, after vaccination, the individual experienced pericarditis (PT: Pericarditis) (Serious: Medically Significant). At the time of reporting, the event outcome of Pericarditis was unknown. Lot number was not provided in the report. No additional information was provided. On 13-APR-2022, additional information was received by Novavax from 4.1(b) reference number 4.1(b) via 4.1(b) The following information was updated in the case: added an additional reporter as 4.1(b) in the general tab, added event start date as 15-MAR-2022 for Pericarditis, and updated event outcome to Not recovered/Not resolved. Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from assessed as possible to considered possible. The sender comment location was moved from the reporter comment field to the sender comment field.				
4.1(b)	0) 13-APR-22 1) 19-APR-22 2) 20-APR-22 3) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 28-MAR-2022	Pericarditis	29-MAR-2022	1: 1	Y	Y	Y
		Regulatory Authority	24	1) Intramuscular	1) -	Not Recovered/Not Resolved	1				

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			Male				1				

Case Narrative

On 01-APR-2022, this serious initial Regulatory Authority Safety Report from 4.1(b) was received via 4.1(b) (Reference number: 4.1(b)) and was received by Novavax via 4.1(b) on 13-APR-2022.

A male of 24 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 28-MAR-2022 in an unspecified vaccination site.

The following medical history was reported: Surgery, Anaphylactic reaction, Eosinophilic esophagitis and Phlebitis.

No concomitant medications were reported.

On 28-MAR-2022, the day of vaccination, the individual experienced arthralgia (PT: Arthralgia) migraine (PT: Migraine), pain in extremity (PT: Pain in extremity), and palpitations (PT: Palpitations).

On 29-MAR-2022, 1 day after vaccination, the individual experienced pericarditis (PT: Pericarditis) (Hospitalization), confusional state (PT: Confusional state), chest pain (PT: Chest pain), fatigue (PT: Fatigue), and musculoskeletal chest pain (PT: Musculoskeletal chest pain).

On 30-MAR-2022, 2 days after vaccination, the individual experienced dysphagia (PT: Dysphagia), and lymphadenopathy (PT: Lymphadenopathy).

On 31-MAR-2022, 3 days after vaccination, the individual experienced chest x-ray (PT: Chest X-ray) (Hospitalization), and electrocardiogram (PT: Electrocardiogram).

Relevant lab tests included: Chest X-ray (Result: Normal; 31-MAR-2022) and Electrocardiogram (Result: Inconclusive; 31-MAR-2022).

On 13-APR-2022, follow-up information with seriousness criteria and hospitalization information were received. The event of Arthralgia was deemed medically significant on 06-APR-2022. Pain in extremity was deemed medically significant on 06-APR-2022. Palpitations was deemed

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

medically significant on 06-APR-2022. Pericarditis was deemed medically significant on 06-APR-2022. Confusional state was deemed medically significant on 06-APR-2022. Chest pain was deemed medically significant on 06-APR-2022. Fatigue was deemed medically significant on 06-APR-2022. Musculoskeletal chest pain was deemed medically significant on 06-APR-2022. Dysphagia was deemed medically significant on 06-APR-2022. Lymphadenopathy was deemed medically significant on 06-APR-2022. Electrocardiogram wad deemed medically significant on 06-APR-2022.

At the time of reporting, the event outcome of Arthralgia was not recovered/not resolved, Chest pain was not recovered/not resolved, Confusional state was not recovered/not resolved, Dysphagia was not recovered/not resolved, Chest X-ray was unknown, Electrocardiogram was unknown, Fatigue was not recovered/not resolved, Lymphadenopathy was recovering/resolving, Migraine was not recovered/not resolved, Musculoskeletal chest pain was not recovered/not resolved, Pain in extremity was not recovered/not resolved, Palpitations was recovered/resolved and event stop date was 28-MAR-2022 and Pericarditis was not recovered/not resolved.

Lot number was not provided in the report.

On 01-APR-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received from a consumer via 4.1(b) reference number 4.1(b)) and was received by Novavax via 4.1(b) on 13-APR-2022. The reporter assessed the causality of the events as Possible.

The 4.1(b) narrative was provided as follows: Refer to the Reaction details Reported Reactions:- Pericarditis (suspected)- Chest pain- Heart palpitations- Dysphagia- Pain below-left collar bone- Migraine/Headache- Swollen painful lymph nodes under the right armpit (Golf ball size)- Pain in right arm/shoulder- Pain in left arm- Joint pain- Fatigue, Brain Fog- Chest X Ray Normal, ECG Inconclusive Medical History: Eosinophilic Esophagitis, Severe Anaphylaxis (Egg, Chick Peas, Others), Severe Phlebitis- Left Arm (Following Surgery in March 2019, since resolved). MPCODECDCN.

On 20-APR-2022, follow-up information was received by Novavax from a patient/consumer in the form of Public Case Details report via 4.1(b) reference number: 4.1(b) no new significant information was provided.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The sender comment was updated from 'were assessed as' to 'is considered'. The sender comment location was moved from the reporter comment field to the sender comment field.									
4.1(b)	0) 13-APR-22 1) 13-APR-22 2) 22-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Pericarditis			Y	Y	Y
		Regulatory Authority	55	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Male								

Case Narrative

On 08-APR-2022, this serious initial Regulatory Authority safety report was receive from a health professional in the form of Public Case Details (PCD) report via 4.1(b) reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 13-APR-2022.

The 4.1(b) narrative was provided as follows: Developed chest pain after Novavax COVID19 Vaccination. Generally well and never had before. Saw cardiologist who deemed it likely pericarditis based on clinical presentation.Had a normal ECG, troponin, echocardiogram, chest X-ray. Commenced on colchicine with minimal improvement 1 month on. Had a few flares of chest pain and presented to hospital emergency department, did not require admission. Ongoing reviews with myself (GP) and cardiologist. Unable to work due to physical job and flares with mild exertion.

On 13-APR-2022, this serious initial Regulatory Authority safety report was receive from health professional in the form of Public Case Details (PCD) report via 4.1(b) reference number: 4.1(b)) via 4.1(b) . The following information was updated in the case: The event outcomes of Chest pain and Pericarditis were reported as not recovered/not resolved.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			On 22-APR-2022, follow-up information was received by Novavax via 4.1(b) reference number: 4.1(b) which was initially received on 08-APR-2022. No new information was received.								
4.1(b)	0) 13-APR-22 1) 19-APR-22 2) 27-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Supraventricular tachycardia	26-FEB-2022		N	Y	Y
		Regulatory Authority	36	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female								

Case Narrative

On 13-APR-2022, this initial non-serious regulatory authority safety report from 4.1(b) was received by Novavax via 4.1(b) reference number: 4.1(b) via 4.1(b) 4.1(b) report entry date was 05-APR-2022.

A female of 36 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On 26-FEB-2022, after vaccination, the individual experienced dyspnoea (PT: Dyspnoea), chest pain (PT: Chest pain), supraventricular tachycardia (PT: Supraventricular tachycardia) and Lethargy (PT: Lethargy).

At the time of reporting, the event outcomes of Chest pain, Dyspnoea, Lethargy and Supraventricular tachycardia were not recovered/not

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			resolved. On 19-APR-2022, non-significant information was received by Novavax via 4.1(b) reference number: 4.1(b). 4.1(b) did not provide an official narrative. No new information was added to the case. No additional information was provided. On 27-APR-2022, a non-significant case correction with Day 0 of 27-APR-2022 was identified. The non-serious case sender comment has been generated since it was missing in the previous version. Reporter information was updated.							
4.1(b)	0) 20-APR-22 1) 25-APR-22 2) 25-APR-22 3) 03-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 04-APR-2022	Pericarditis	06-APR-2022	UNK: 2	Y	Y	Y
		Regulatory Authority	25	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Male				2				
	0) 20-APR-22 1) 25-APR-22 2) 25-		Adult	NUVAXOVID / Injection	UNK: 04-APR-2022	Electrocardiogram abnormal			N	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	APR-22 3) 03-MAY-22										
			25 Male	1) Intramuscular	1) -	Unknown					

Case Narrative

On 11-APR-2022, an initial serious Regulatory Authority safety report was received from a Pharmacist in the form of Public Case Details (PCD) report from 4.1(b) reference number- 4.1(b)) via 4.1(b) and received by Novavax on 20-APR-2022.

The 4.1(b) narrative was provided as follows: Patient presented to ED with chest pain following COVID-19 Novovax (Booster) vaccination. Previously diagnosed with pericarditis following COVID-19 Pfizer vaccination (second dose) in October of 2021 which was treated with colchicine and NSAIDs. Bloods CXR and ECG performed today in ED- patient diagnosed with recurrent pericarditis. COVID Team: 2/7 post vaccination developed mild chest pain palpitations and SOB. Presented to ED due to hx of Pericarditis. Stayed in ED for 4-5 hrs. ECG - global STE Troponin 4 CRP 33 D/c on Colchicine and Ibuprofen. Client states some improvement but ongoing symptoms. Other vaccines in the last 4 weeks: N Allergies: Y Illness at the time of vaccination: N.

On 25-APR-2022, a significant follow-up information was received by Novavax via 4.1(b) reference number: 4.1(b)). The following information was updated in the case: concomitant medication as Comirnaty Covid-19 vaccine (tozinameran); Additional events were reported: C-reactive protein increased (PT: C-reactive protein increased), Electrocardiogram abnormal (PT: Electrocardiogram abnormal) and Troponin T (PT: Troponin T).

Additional information was not provided.

On 27-APR-2022, a significant case correction with day 0 of 25-APR-2022 was identified. The following information was updated: Follow-up dates were added in the general tab and narrative was updated.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		On 03-MAY-2022, it was identified that manufacturer control number (MCN) 4.1(b) is a duplicate to this case 4.1(b). The information from 4.1(b) has been added to this case, 4.1(b). This case, 4.1(b) will be retained and 4.1(b) will be invalidated.									
4.1(b)	0) 20-APR-22 1) 26-APR-22 2) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 28-MAR-2022	Pericarditis	2022		Y	Y	Y
		Regulatory Authority	24	1) Intramuscular	1) -	Unknown					
			Male								

Case Narrative

On 12-APR-2022, this serious initial Regulatory Authority safety report was receive from a consumer in the form of Public Case Details (PCD) report via 4.1(b) reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 20-APR-2022.

The 4.1(b) narrative was provided as follows: Refer to the Reaction details Reported Reactions: - Pericarditis (suspected) - Chest pain - Heart palpitations - Dysphagia - Pain below left collar bone - Migraine / Headache - Swollen painful lymph nodes under right armpit (Golf ball size) - Pain in right arm/right shoulder - Pain in left arm - Joint pain - Fatigue, Brain Fog - Chest X Ray Normal, ECG Inconclusive. Arthralgia; Chest pain; Chest X-ray; Confusional state; Dysphagia; Electrocardiogram; Fatigue; Lymphadenopathy; Migraine; Musculoskeletal chest pain; Pain in extremity; Palpitations; Pericarditis. Previous vaccine reactions: No NA Hx: Unknown

On 12-APR-2022, follow-up information was received via 4.1(b) reference number: 4.1(b)) and was received by Novavax on 26-APR-2022. No new information was received.

Based on internal review on 17-MAY-2022, a non-significant case correction was identified. The following updates to the sender comment were

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	made: The causality was updated from assessed as to considered. The sender comment location was moved from the reporter comment field to the sender comment field.										
4.1(b)	0) 20-APR-22 1) 27-APR-22 2) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 24-MAR-2022	Myocarditis			Y	Y	Y
		Regulatory Authority	39	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female								

Case Narrative

On 13-APR-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received from a consumer in the form of Public Case Details (PCD) report from 4.1(b) reference number 4.1(b)) via 4.1(b) and was received by Novavax on 20-APR-2022.

The regulatory authority narrative was provided as follows:
Local Reaction - Pain; Swelling which extended past elbow or shoulder; Headache; Joint aches/pain; Vomiting; Fatigue/tiredness. ADDED from Mgt of Event unstructured: Outcome is unknown but ongoing. Further details as provided: Ongoing symptoms, Days missed from work etc: 3 or more days. Previous vaccine reactions: No NA

On 27-APR-2022, additional information was received by Novavax from 4.1(b) reference number 4.1(b)). The following information has been updated in the case: An additional reporter (4.1(b) was added to the case.

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		The causality was updated from assessed as possible to is considered possible. The sender comment location was moved from the reporter comment field to the sender comment field.									
4.1(b)	0) 20-APR-22 1) 27-APR-22 2) 31-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	1: UNK 2: 24-MAR-2022	Electrocardiogram abnormal	04-APR-2022	2: 11	Y	Y	Y
		Regulatory Authority	31	1) Intramuscular 2) Intramuscular	1) - 2) -	Unknown					
			Male				11				
							11				
	0) 20-APR-22 1) 27-APR-22 2) 31-MAY-22		Adult	NUVAXOVID / Injection	1: UNK 2: 24-MAR-2022	Pericarditis	04-APR-2022	2: 11	Y	Y	Y
			31	1) Intramuscular 2) Intramuscular	1) - 2) -	Not Recovered/Not Resolved					
			Male				11				
							11				

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	0) 20-APR-22 1) 27-APR-22 2) 31-MAY-22		Adult	NUVAXOVID / Injection	1: UNK 2: 24-MAR-2022	Troponin increased	04-APR-2022	2: 11	Y	Y	Y
			31	1) Intramuscular 2) Intramuscular	1) - 2) -	Unknown					
			Male				11				
							11				

Case Narrative

On 13-APR-2022, this serious initial Regulatory Authority safety report was received from a health professional in the form of Public Case Details (PCD) report via 4.1(b) Reference number 4.1(b)) via 4.1(b) and was received by Novavax on 20-APR-2022.

The 4.1(b) narrative was provided as follows: Chest pains developed Monday 4/4/22 Tight, feeling, sharp pain. Pleuritic component worse on deep inspiration. Had second dose Novavax 24/3/22 Went to DEM: Troponin = 5. ECG in DEM apparently was normal. Examination: Cardiovascular: Heart sounds: x2 Murmur: No murmurs No pericardial rub heard. Not exquisitely tender over costochondral joints. Some tenderness around left midclavicular line. Does work on a manual job so new muscle strain could be working aetiology. ECG: Large peaked T waves V3 through V6 with ST elevation in V3 and V4. ST elevation in lead II and aVF. Unlikely ischaemia much more likely related to pericarditis.

On 27-APR-2022, follow-up information was received by Novavax in the form of a Regulatory Authority Safety Report from 4.1(b) via 4.1(b) reference number: 4.1(b) which was received on 13-APR-2022. No new information was received.

On 31-MAY-2022, it was identified that manufacturer control number (MCN) 4.1(b) , is a duplicate to this case, 4.1(b) The information from 4.1(b) has been added to this case, 4.1(b) . This case, 4.1(b) will be retained and 4.1(b) will be invalidated.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		The following information was added to this case: The patient's age was updated to 31 years old (previously reported as 30-years), the event of "Electrocardiogram" was updated to the event of "Electrocardiogram abnormal" and the event of "Troponin" updated to "Troponin increased". Date of troponin and ECG in laboratory data was updated to 04-APR-2022 and a separate entry for 'ECG in DEM (Division of Emergency Management) apparently was normal' was added for 04-APR-2022. The seriousness criteria of hospitalization was added for the events of Chest pain, Electrocardiogram abnormal, Musculoskeletal chest pain, Pericarditis and Troponin increased as the individual was admitted to hospital for management of event on an unspecified date in 2022. The 4.1(b) narrative was provided as follows: A Male patient exhibited the following symptom(s) for the duration(s) noted: Chest pain Electrocardiogram Electrocardiogram ST segment elevation Musculoskeletal chest pain Pericarditis Troponin from 04/04/2022; Chest pains developed monday 4/4/22 Tight; feeling; sharp pain. Pleuritic component worse on deep inspiration. Had second dose Novavax 24/3/22 Went to DEM: Troponin = 5. ECG in DEM apparently was normal. Examination: Cardiovascular: Heart sounds: x2 Murmur: No murmurs No pericardial rub heard. Not exquisitely tender over costochondral joints. Some tenderness around left midclavicular line. Does work on a manual job so new muscle strain could be working aetiology. ECG: Large peaked T waves V3 through V6 with ST elevation in V3 and V4. ST elevation in lead II and aVF. Unlikely ischaemia much more likely related to pericarditis. Patient was managed by Hospital emergency department. Hospital. Patient medical history includes at the time of vaccination patient was not ill. This AEFI was sent to the Vaccine Clinical Triage Group for review.									
4.1(b)	0) 20-APR-22 1) 27-APR-22 2) 20-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 08-APR-2022	Troponin increased	08-APR-2022	UNK: 0	N	Y	Y
		Regulatory Authority	50	1) Intramuscular	1) -	Recovering/Resolving					
			Female				0				

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
Case Narrative											
[redacted]	0) 20-APR-22 1) 28-APR-22 2) 17-MAY-22	[redacted]	Adult	NUVAXOVID / Injection	1: 05-APR-2022	Pericarditis	06-APR-2022	1: 1	Y	Y	Y

On 13-APR-2022, this initial non-serious Regulatory Authority safety report from [redacted] was received from a consumer in the form of Public Case Details (PCD) report from [redacted] Reference number: [redacted]) via [redacted] and was received by Novavax on 20-APR-2022.

The [redacted] narrative was provided as follows:
Experienced heart palpitations on evening of 8 April. More palpitations on 9 April, experienced sudden chest pain on morning 10 April, continued with intermittent heart palpitations and chest pain. Experienced chest pain on Tuesday 12 April, did not abate and felt generally unwell. Woke up with chest pain and decided to go to emergency to get it checked out. Reported reaction: Chest pain, heart palpitations, troponin level of 47 Hx: Myocarditis and pericarditis as a result of first COVID-19 vaccine administered on 29 November 2021 Moderna.

On 25-APR-2022,as per the email received from Medical Review, the events Myocarditis and Pericarditis have been captured as medical history and removed from the event tab. Also, Moderna is retained as co-suspect.

On 13-APR-2022, follow-up information was received via [redacted] reference number: [redacted]) and was received by Novavax on 27-APR-2022. No new information was received.
On 25-APR-2022,as per the email received from Medical Review, Myocarditis and Pericarditis have not been captured as adverse events to Nuvaxovid.

On 29-APR-2022, a significant case correction with Day 0 of 20-APR-2022 was identified. The following information was updated: Overall case seriousness was changed from serious to non-serious and the first sentence of the narrative was updated from "this serious initial" to "this non-serious initial."

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		Regulatory Authority	24	1) Intramuscular	1) -	Not Recovered/Not Resolved	1				
			Female								
							1				
	0) 20-APR-22 1) 28-APR-22 2) 17-MAY-22		Adult	NUVAXOVID / Injection	1: 05-APR-2022	Troponin increased	09-APR-2022	1: 4	Y	Y	Y
			24	1) Intramuscular	1) -	Unknown	4				
			Female								
							4				
	0) 20-APR-22 1) 28-APR-22 2) 17-MAY-22		Adult	NUVAXOVID / Injection	1: 05-APR-2022	Myocarditis			Y	Y	Y
			24	1) Intramuscular	1) -	Unknown					
			Female								

Case Narrative

On 14-APR-2022, this initial serious Regulatory Authority safety report from 4.1(b) was received from a patient/consumer in the form of Public Case Details report from 4.1(b) Reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 20-APR-2022.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
4.1(b)	0) 20-APR-22 1) 26-APR-22 2) 06-MAY-22 3) 11-	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 02-MAR-2022	Pericarditis	16-MAR-2022	UNK: 14	Y	Y	Y

The 4.1(b) narrative was provided as follows: I began experiencing a stabbing chest pain, pressure and heart palpitations on April 6th 2022. Last Thursday I jogged for a couple minutes to get out of the rain with my dog and feltlike I was having a heart attack. I was sent to the hospital (9/4) where they gave me an ECG and blood tests. ECG was all clear and blood tests were mostly normal with slight inflammatory markers and troponin levels slightly high. ED Doctors said they thought it was mild pericarditis. Was told to see a doctor a week after if it continues, and to diagnose, which is what I've done today to run more tests. I have a referral for a chest x-ray and a few other things. Reported reactions: Chest pain, chest pressure, costochondritis, heart palpitation.

On 28-APR-2022, follow-up was received by Novavax from 4.1(b) 4.1(b) reference number: 4.1(b) . The following information was added to the case: An additional reporter and event were added to the case. On an unspecified date, after vaccination, the individual experienced myocarditis (PT: Myocarditis) (Serious: Medically Significant). At the time of reporting, the event outcome of Myocarditis was unknown. No additional information was provided.

On 17-MAY-2022, a non-significant case correction was identified. The following information was updated:The follow-up introductory statement should be updated to: "On 28-APR-2022, follow-up was received by Novavax via 4.1(b) reference number: 4.1(b)) and was received by 4.1(b) on 14-APR-2022". In the Lab details, Inflammatory marker test result was updated to "Slightly high". The sender's comment was updated to- "Based on the spontaneous nature of the report, the causal relationship between Nuvaxovid and Chest discomfort, Nuvaxovid and Chest pain, Nuvaxovid and Costochondritis, Nuvaxovid and Inflammatory marker increased, Nuvaxovid and Myocarditis, Nuvaxovid and Palpitations, Nuvaxovid and Pericarditis and Nuvaxovid and Troponin increased is considered as Possible".

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	MAY-22 4) 16-MAY-22										
		Regulatory Authority	34	1) Intramuscular	1) -	Recovered/Resolved					
			Female								
							14				
	0) 20-APR-22 1) 26-APR-22 2) 06-MAY-22 3) 11-MAY-22 4) 16-MAY-22		Adult	NUVAXOVID / Injection	UNK: 02-MAR-2022	Electrocardiogram abnormal	18-MAR-2022	UNK: 16	N	Y	Y
			34	1) Intramuscular	1) -	Unknown					
			Female								
							16				

Case Narrative

On 12-APR-2022, this initial, serious, regulatory authority safety report from 4.1(b) was received from a physician in the form of Public Case Details report via 4.1(b) reference number: 4.1(b)) and was received by Novavax on 20-APR-2022 via 4.1(b)

The 4.1(b) narrative was provided as follows:

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
4.1(b)	0) 20-APR-22 1) 25-APR-22 2) 26-APR-22 3) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Extrasystoles	14-MAR-2022		N	Y	Y
		Regulatory Authority	42	1) Intramuscular	1) -	Not Recovered/Not Resolved					

Felt generally unwell re headaches and joint pains after 1st novavax dose but approx 2/52 after same developed chest pains and SOB -assessed ED 17 and 18/3/22 and ecg changes seen by cardiologist and advised probable pericarditis - ongoing symptoms btu outpatient echo (25/03/2022) stable re no myocarditis/pericarditis seen then, mild tricuspid regurg only. ADDED from Mgt of Event unstructured: Outcome is unknown but ongoing. Further details as provided: still ongoing symptoms- chest pains easing but not resolved - SOB improved- still generalised aches and severe fatigue Ethnic sub group unstructured:Unknown Previous vaccine reactions: No NA Hx: Unknown

On 26-APR-2022, follow-up information was received by Novavax in the form of a Regulatory Authority Safety Report from 4.1(b) via 4.1(b) reference number: 4.1(b)) which was received on 12-APR-2022. No new information was received.

On 04-MAY-2022, non- significant case correction was identified. The following information was added: Reporter information was updated. Causality statement was added to the narrative "The reporter assessed the causality as possible".

On 11-MAY-2022, non-significant case correction was identified. The following information was added: The sender comment was updated.

On 16-MAY-2022, non-significant case correction was identified. The following information was added: The sender comment which inadvertently was captured under the reporter comment field was moved to the sender comment field and the reporter comment field was left blank.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			Male								

Case Narrative

On 11-APR-2022, a non-serious initial Regulatory Authority Safety Report from 4.1(b) was received from a consumer in the form of public case details report via 4.1(b) (Reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 20-APR-2022.

A male of 42 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

The following concomitant medications were reported: Comirnaty.

On 14-MAR-2022, after vaccination, the individual experienced asthenia (PT: Asthenia), dizziness (PT: Dizziness), extrasystoles (PT: Extrasystoles), tachycardia (PT: Tachycardia), nausea (PT: Nausea), palpitations (PT: Palpitations), and fatigue (PT: Fatigue).

At the time of reporting, the event outcome of Asthenia, Dizziness, Extrasystoles, Fatigue, Nausea, Palpitations and Tachycardia were not recovered/not resolved.

Lot number was not provided in the report.

On 25-APR-2022, follow-up information was received by Novavax from a patient/consumer in the form of Public Case Details report via 4.1(b) reference number 4.1(b)) via 4.1(b) . No significant information was received.

On 26-APR-2022, a non-significant case correction was identified. The following information was updated:

On 25-Apr-2022, follow-up information was received from 4.1(b) No new information was provided."

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			made: The causality was updated from were assessed as possible to were considered possible. The sender comment location was moved from the reporter comment field to the sender comment field.								
4.1(b)	0) 20-APR-22 1) 21-APR-22 2) 28-APR-22 3) 05-MAY-22 4) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Supraventricular tachycardia	19-FEB-2022		N	Y	Y
		Regulatory Authority	50	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female								

Case Narrative

On 14-APR-2021, an initial regulatory authority report from 4.1(b) was received by 4.1(b) reference number 4.1(b)) and was received by Novavax via 4.1(b) on 20-APR-2022.

A female of 50 years was vaccinated with an unspecified primary dose of intramuscular Nuvaxovid 10 ug/mL on an unspecified date.

No medical history or concomitant medications were reported.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
4.1(b)	0) 20-APR-22 1) 28-APR-22 2) 17-	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Pericardial effusion	18-FEB-2022		Y	Y	Y

On 19-FEB-2022, after vaccination, the individual experienced supraventricular tachycardia (PT: Supraventricular tachycardia), asthenia (PT: Asthenia), nausea (PT: Nausea), dizziness (PT: Dizziness), dyspnoea (PT: Dyspnoea) and chest pain (PT: Chest pain).

At the time of reporting, the event outcomes of supraventricular tachycardia, asthenia, chest pain, dizziness, dyspnoea and nausea were not recovered/not resolved.

Lot number was not provided in the report.

On 21-APR-2022, a non-significant case correction was identified. The following information was updated: Reporter information was added and Senders comment was updated to match the template for spontaneous cases.

On 28-APR-2022, follow-up information was received by Novavax from 4.1(b) reference number: 4.1(b)). No additional information was reported.

On 05-MAY-2022, a non-significant case correction was identified. The following information was updated: Reporter details were erroneously captured in the initial narrative. These details have been removed.

Based on Internal review on 17-May-2022, a non- significant case correction was identified. The follow updates to the sender comment were made:

The causality was updated from were assessed as possible to is considered possible.
The sender comment location was moved from the reporter comment field to the sender comment field.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	MAY-22										
		Regulatory Authority	42	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Male								
	0) 20-APR-22 1) 28-APR-22 2) 17-MAY-22		Adult	NUVAXOVID / Injection	UNK: UNK	Pericarditis			Y	Y	Y
			42	1) Intramuscular	1) -	Unknown					
			Male								

Case Narrative

On 14-APR-2022, this initial serious regulatory authority safety report from 4.1(b) was received via the 4.1(b) -reference 4.1(b)) and was received by Novavax on 20-APR-2022 via 4.1(b) 4.1(b) did not provide a narrative.

A male of 42 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On 18-FEB-2022, after vaccination, the individual experienced pericardial effusion (PT: Pericardial effusion) (Serious: Medically Significant), chest

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				pain (PT: Chest pain) and dizziness (PT: Dizziness). At the time of reporting, the event outcome of Chest pain, Dizziness and Pericardial effusion was not recovered/not resolved. Lot number was not provided in the report. No additional information was provided. On 28-APR-2022, follow-up information was received by Novavax in the form of a Regulatory Authority Safety Report from 4.1(b) via 4.1(b) reference number 4.1(b) which was received on 14-APR-2022. Following information was updated in the case: Events Panic reaction (PT: Panic reaction), Pericarditis (PT: Pericarditis) (Serious: Medically Significant) and Troponin (PT: Troponin) were added. Based on Internal review on 17-May-2022, a non- significant case correction was identified. The follow updates to the sender comment were made: The causality was updated from were assessed as possible to is considered possible. The sender comment location was moved from the reporter comment field to the sender comment field.				
4.1(b)	0) 27-APR-22 1) 06-MAY-22 2) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 10-MAR-2022	Pericarditis	25-MAR-2022	UNK: 15	Y	Y	Y
		Regulatory Authority	36	1) Intramuscular	1) -	Not Recovered/Not Resolved					

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			Male				15				

Case Narrative

On 22-APR-2022, this initial serious Regulatory Authority safety report from 4.1(b) was received from a physician by 4.1(b) reference number: 4.1(b)) and was received by Novavax on 27-APR-2022 via 4.1(b)

The 4.1(b) narrative was provided as follows:
Patient had left sided chest pain about 15-16 days after vaccination , got worse and presented to ED Hospital 22/04/2022 spoken to vaccinee Symptoms commenced ~2 weeks post vaccination, chest pain, no SOB or palpitations. Worsen with exertion. Attended ED on 28/03/2022 where bloods, ECG, ECHO was done. Colchicine (for 3months) and ibuprofen (for 2 weeks) prescribed. For outpatient cardio review due in June 2022. attended hospital again on 16/04/2022 for chest pain. SIS discussed, interested mainly for medical contraindication. ADDED from Mgt of Event unstructured: Outcome is unknown but ongoing. Further details as provided: Patient is on medical management of Pericarditis. he will be seeing cardiologist for a follow up. Previous vaccine reactions: No NA Outcome is unknown but ongoing. Further details as provided: Patient is on medical management of Pericarditis. he will be seeing cardiologist for a follow up. Previous vaccine reactions: No NA

On 06-MAY-2022, follow-up was received by Novavax from 4.1(b) reference number: 4.1(b). No additional information was reported.

Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from were assessed as possible to was considered possible
The sender comment location was moved from the reporter comment field to the sender comment field.

4.1(b)	0) 11-MAY-22 1) 12-MAY-22 2) 19-	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 15-MAR-2022	Myocarditis		Y	Y	Y

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	MAY-22 3) 19-MAY-22										
		Regulatory Authority	32	1) Intramuscular	1) -	Unknown					
			Male								

Case Narrative

On 05-MAY-2022, this serious initial Regulatory Authority safety report from 4.1(b) was received from a consumer via 4.1(b) reference number 4.1(b)), via 4.1(b) and was received by Novavax on 11-MAY-2022.

The Therapeutic Goods Administration narrative was provided as follows:
Stomach ulcer, Post vaccine - chronic fatigue syndrome, Post vaccine -postural, orthostatic tachycardia syndrome, Post vaccine myocarditis, Post vaccine tachycardia. Previous vaccine reactions: No NA

On 12-MAY-2022, a non-significant case correction was identified. The following information was updated in the case: To align with the DEM Sender Comment template (Based on the spontaneous nature of the report, the causal relationship between PRIMARY SUSPECT PRODUCT and the reported event(s) is considered CAUSALITY AS DETERMINED RESULT), "were assessed as possible" was corrected to "is considered possible".

On 19-MAY-2022, follow-up information was received by Novavax via 4.1(b) reference number: 4.1(b) received the report on 05-MAY-2022. No new information was received.

On 23-MAY-2022, a significant case correction with Day 0 of 19-MAY-2022 was identified. The following information was updated: The sender comment was moved to the appropriate location (previously in the reporter comment field).

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 18-MAY-22 1) 26-MAY-22	4.1(b)	Elderly	NUVAXOVID / Injection	UNK: UNK	Supraventricular extrasystoles	03-MAR-2022		N	Y	Y
		Regulatory Authority	69	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female								

Case Narrative

On 12-MAY-2022, this non-serious initial regulatory authority safety report from 4.1(b) was received via 4.1(b) 4.1(b) reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 18-MAY-2022.

A female of 69 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On 03-MAR-2022, after vaccination, the individual experienced chest pain (PT: Chest pain), myalgia (PT: Myalgia) and supraventricular extrasystoles (PT: Supraventricular extrasystoles).

At the time of reporting, the event outcomes of Chest pain, Myalgia and Supraventricular extrasystoles were not recovered/not resolved.

Lot number was not provided in the report.

No additional information was provided.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		On 26-MAY-2022, additional information was received by Novavax via 4.1(b) reference number: 4.1(b) received the report on 12-MAY-2022. No new information was received.									
4.1(b)	0) 18-MAY-22 1) 30-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: UNK	Carditis	06-APR-2022		Y	Y	Y
		Regulatory Authority	43	1) Intramuscular	1) -	Recovering/Resolving					
			Female								

Case Narrative

On 14-MAY-2022, this serious initial Regulatory Authority safety report from 4.1(b) was received via 4.1(b) reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 18-MAY-2022.

A female of 43 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with an unspecified primary dose on an unspecified date.

No medical history was reported.

No concomitant medications were reported.

On 06-APR-2022, after vaccination, the individual experienced cardiac disorder (PT: Cardiac disorder), carditis (PT: Carditis) (Serious: Medically Significant), chest pain (PT: Chest pain), fatigue (PT: Fatigue), headache (PT: Headache), heart rate irregular (PT: Heart rate irregular), hyperaesthesia (PT: Hyperaesthesia), influenza like illness (PT: Influenza like illness), injection site pain (PT: Injection site pain), nausea (PT: Nausea) and pyrexia (PT: Pyrexia).

At the time of reporting, the events outcome of Cardiac disorder, Carditis, Chest pain, Fatigue, Headache, Heart rate irregular, Hyperaesthesia, Influenza like illness, Injection site pain, Nausea and Pyrexia were recovering/resolving.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				Lot number was not provided in the report. No additional information was provided. On 30-MAY-2022, follow-up information was received by Novavax from 4.1(b) reference number: 4.1(b). 4.1(b) received the report on 14-MAY-2022. On an unspecified date, after vaccination the individual experienced exercise tolerance decreased (PT: Exercise tolerance decreased). At the time of reporting, the event outcome of Exercise tolerance decreased was unknown.							
4.1(b)	0) 19-MAY-22	4.1(b)	Elderly	NUVAXOVID / Injection	UNK: UNK	Myopericarditis			Y	Y	Y
		Regulatory Authority	76	1) Intramuscular	1) -	Unknown					
			Female								
	0) 19-MAY-22		Elderly	NUVAXOVID / Injection	UNK: UNK	Troponin increased			N	Y	Y
			76	1) Intramuscular	1) -	Unknown					
			Female								
Case Narrative				On 06-MAY-2022, this serious, initial, Regulatory Authority Safety report from 4.1(b) was received via 4.1(b): Reference number 4.1(b)) and was received by Novavax on 20-MAY-2022. A female of 76 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on an unspecified date. The following secondary suspect medications were reported: Comirnaty (tozinameran) with an unspecified dose and dosing frequency. No medical history was reported.							

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				Concomitant medications included: Aspirin (acetylsalicylic acid), atorvastatin (tradename not specified), hydralazine hydrochloride(tradename not specified), mirtazapine (tradename not specified), telmisartan (tradename not specified), Bisoprolol (bisoprolol fumarate), Covid-19 Vaccine Astrazeneca and Symbicort Turbuhaler 200/6 (budesonide;formoterol(eformoterol)fumaratedihydrate). On an unspecified date, after vaccination, the individual experienced abdominal pain (PT: Abdominal pain), cardiomyopathy (PT: Cardiomyopathy) (Serious: Medically Significant), chest pain (PT: Chest pain), dyspnoea (PT: Dyspnoea), electrocardiogram normal (PT: Electrocardiogram normal), fibrin d dimer increased (PT: Fibrin D dimer increased), left ventricular end-diastolic pressure increased (PT: Left ventricular end-diastolic pressure increased), myopericarditis (PT: Myopericarditis) (Serious: Medically Significant), troponin increased (PT: Troponin increased) and urinary tract infection (PT: Urinary tract infection). At the time of reporting, the event outcomes of Abdominal pain, Cardiomyopathy, Chest pain, Dyspnoea, Electrocardiogram normal, Fibrin D dimer increased, Left ventricular end-diastolic pressure increased, Myopericarditis, Troponin increased and Urinary tract infection were unknown. Lot number was not provided in the report. No additional information was reported.				
4.1(b)	0) 25-MAY-22 1) 01-JUN-22 2) 02-JUN-22 3) 14-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 17-FEB-2022	Pericarditis	20-FEB-2022	1: 3	Y	Y	Y
		Regulatory Authority	29	1) Intramuscular	1) -	Not Recovered/Not	3				

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
						Resolved					
			Male								
							3				
Case Narrative	On 18-MAY-2022, this initial, serious regulatory authority safety report from 4.1(b) was received from a patient via 4.1(b) reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 25-MAY-2022. The 4.1(b) narrative was provided as follows: Felt pain in left chest within 4 days of first dose of Vaccination. Attended Emergency and GP. Multiple scans and blood tests. Clinical Diagnosis of Pericarditis end of April. Not resolved. Follow up received 19/05/2022 Ongoing Continuous ache in left chest / shoulder / arm, sharp stabbing pains in heart area under ribs, fatigue, shortness of breath. Seen in emergency, by GP and Cardiologist. I don't have copies of these records (pathology and imaging) on file, most came back fine I believe but was given clinical diagnosis from Cardiologist. On 01-JUN-2022, follow-up information was received by Novavax via 4.1(b) reference number 4.1(b)) 4.1(b) received the report on 18-MAY-2022. No new information was received. On 02-JUN-2022, a non-significant case correction was identified. The following information was updated: A partial date of 2022 was added for the multiple scans and blood test in the lab section. On 14-JUN-2022, it was identified that manufacturer control number (MCN) 4.1(b) is a duplicate to this case, 4.1(b) . The information from 4.1(b) has been added to this case, 4.1(b) . This case, 4.1(b) will be retained and 4.1(b) be invalidated.										
4.1(b)	0) 08-JUN-22 1) 08-JUN-22 2) 10-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 18-APR-2022	Myocarditis	APR-2022		Y	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	3) 15-JUN-22										
		Regulatory Authority	23	1) Intramuscular	1) -	Unknown					
			Female								

Case Narrative

On 01-JUN-2022, this serious, initial Regulatory Authority safety report from 4.1(b) was received from a reporter (Other) via 4.1(b) ; Reference Number: 4.1(b)) via 4.1(b) and was received by Novavax on 08-JUN-2022.

The 4.1(b) narrative was provided as follows:
Chest pain - background of myocarditis Previous vaccine reactions: No NA Hx: Unknown.

On 09-JUN-2022, a significant case correction with Day 0 of 08-JUN-2022 was identified. The following information was updated: The sender comment was included in the sender comm ent field.

On 10-JUN-2022, follow-up information was received by Novavax via the 4.1(b) reference number: 4.1(b)) via 4.1(b) received the report on 01-JUN-2022. Reporter details were updated.

On 15-JUN-2022, follow-up information was received by Novavax via the 4.1(b) reference number: 4.1(b) . 4.1(received the report on 01-JUN-2022. The following information was updated: an additional reporter was added and the individual's age was updated from 24 years to 23 years.

4.1(b)	0) 15-JUN-22 1) 15-JUN-22 2) 27-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 05-MAY-2022	Pericarditis	14-MAY-2022	UNK: 9	Y	Y	Y

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		Regulatory Authority	40	1) Intramuscular	1) -	Unknown					
			Female								
							9				

Case Narrative

On 08-JUN-2022 , this serious inittial Regulatory Authority report from 4.1(b) was received from a physician via 4.1(b) [redacted]) via 4.1(b) and was received by Novavax on 15-JUN-2022. 4.1(b) [redacted] provided the following narrative:

sob post novavax, peri Ethnic sub group unstructured: Unknown Previous vaccine reactions: No NA Hx: Unknown.

Lot number was not provided in the report.

No additional information is expected.

On 17-JUN-2022, a significant case correction with Day 0 of 15-JUN-2022 was identified. The following information was updated: (case narrative).
On 08-JUN-2022 , this serious initial Regulatory Authority report from 4.1(b) was received from a physician via 4.1(b) [redacted] and was received by Novavax on 15-JUN-2022. A female of 40 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose (dose number unspecified) on 05-MAY-2022. No medical history was reported. No concomitant medications were reported. On 14-MAY-2022, 10 days after vaccination, the individual experienced dyspnoea (PT: Dyspnoea) (required hospital emergency department), pericarditis (PT: Pericarditis) (Serious: Medically Significant). At the time of reporting, the event outcomes of Pericarditis and Dyspnoea were unknown. Lot number was not provided in the report. No additional information is expected.

The 4.1(b) [redacted] narrative was provided as follows:
sob post novavax, peri Ethnic sub group unstructured: Unknown Previous vaccine reactions: No NA Hx: Unknown.

On 27-JUN-2022, follow-up information was received by Novavax via 4.1(b) [redacted] reference number: 4.1(b) [redacted] received the report on 08-JUN-2022. No new information was received.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 22-JUN-22 1) 05-JUL-22	4.1(b)	Adult	NUVAXOVID / Injection	1: 19-MAY-2022	Myocarditis	23-MAY-2022	1: 4	Y	Y	Y
		Regulatory Authority	44	1) Intramuscular	1) -	Not Recovered/Not Resolved	4				
			Female				4				
	0) 22-JUN-22 1) 05-JUL-22		Adult	NUVAXOVID / Injection	1: 19-MAY-2022	Electrocardiogram abnormal	JUN-2022		N	Y	Y
			44	1) Intramuscular	1) -	Unknown					
			Female								

Case Narrative

On 17-JUN-2022, this serious initial Regulatory Authority safety report from 4.1(b) was received from a patient/consumer via 4.1(b) reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 22-JUN-2022.

A female of 44 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 19-MAY-2022.

The following medical history was reported: COVID-19, Heart rate decreased, Atrial fibrillation and Fibromyalgia. Illness at the time of vaccination was reported as nil.

The following concomitant medications were reported: Tambocor (flecainide acetate).

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

On 19-MAY-2022, after vaccination, the individual experienced fatigue (PT: Fatigue) and pain in extremity (PT: Pain in extremity). On 23-MAY-2022, four days after vaccination, the individual experienced asthenia (PT: Asthenia), cardiac flutter (PT: Cardiac flutter) (Serious: Medically Significant), concomitant disease aggravated (PT: Concomitant disease aggravated), dizziness (PT: Dizziness), myocarditis (PT: Myocarditis) (Serious: Medically Significant) and palpitations (PT: Palpitations). On an unspecified date in MAY-2022, after vaccination, the individual experienced arthralgia (PT: Arthralgia) and dyspnoea (PT: Dyspnoea). On an unspecified date in JUN-2022, after vaccination, the individual experienced electrocardiogram abnormal (PT: Electrocardiogram abnormal). On an unspecified date in 2022, after vaccination, the individual experienced abdominal discomfort (PT: Abdominal discomfort).

The management of event for concomitant disease aggravated was reported to be a general practitioner (GP) assessment.

Relevant lab tests included: Electrocardiogram (Result: ECG looked a bit wonky, and stated it may be a case of myocarditis; 07-JUN-2022).

At the time of reporting, the event outcomes of Abdominal discomfort, Cardiac flutter, Concomitant disease aggravated, Dizziness and Myocarditis were not recovered/not resolved; the event outcomes of Asthenia, Fatigue, Pain in extremity and Palpitations were recovering/resolving, and the event outcomes of Arthralgia, Dyspnoea and Electrocardiogram abnormal were unknown.

Action taken with Tambocor (flecainide acetate) was reported as dose increased.

Lot number was not provided in the report.

No additional information was provided.

4.1(b) [redacted] narrative was provided as follows:

In January 2022 I had was given a 6 month exemption for having had covid-19. For the first 3 days following 1st novovax aside form sore arm and a bit of fatigue I felt relatively okay. On day 4 I started experiencing dizziness and random heart flutters along with arrhythmia. Generally my resting heart rate is quite low but at night time, bed time when resting about to fall asleep my heart rate has been incredibly fast along with bouts

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				of AF being irregular. I have had extreme fatigue, joint pain, zero energy and felt like I have limited breath or lung capacity. It has now been 4 weeks since my first Novavax and whilst the fatigue is slowly improving I am still having irregularities of my heart, dizzy spells and upset stomach. On the 7th June I contacted my GP practice but my GP was on leave, I attended clinic and was seen by another doctor. Explained symptoms, put on ECG and told my ECG looked a bit wonky, and stated it may be a case of myocarditis. Medical Hx: Diagnosed atrial fibrillation and fibromyalgia. Nil illness at time of vaccination. On 05-JUL-2022, follow-up information was received by Novavax via 4.1(b) reference number: 4.1(b) received the report on 17-JUN-2022. No new information was received. The initial narrative should have included the reporter causality of the events as Possible.						
4.1(b)	0) 29-JUN-22 1) 05-JUL-22	4.1(b)		NUVAXOVID / Injection	UNK: 06-APR-2022	Troponin increased	20-APR-2022	UNK: 14	N	Y	Y
		Regulatory Authority	Unknown	1) Intramuscular	1) -	Recovered/Resolved					
			Female				14				
Case Narrative				On 21-JUN-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received from a pharmacist via the 4.1(b) reference number: 4.1(b)) via 4.1(b) and was received by Novavax on 29-JUN-2022. A female of 76 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose unspecified on 06-APR-2022. No medical history was reported. The following concomitant medications were reported: Aspirin (acetylsalicylic acid), atorvastatin, bisoprolol, hydralazine hydrochloride, mirtazapine, Symbicort Turbuhaler (budesonide, formoterol fumarate) 200/6, and telmisartan.						

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

On 20-APR-2022, after vaccination, the individual experienced chest pain (PT: Chest pain) (Serious: Hospitalization), C-reactive protein increased (PT: C-reactive protein increased), urinary tract infection (PT: Urinary tract infection), escherichia test positive (PT: Escherichia test positive), troponin increased (PT: Troponin increased), and abdominal pain upper (PT: Abdominal pain upper).

The individual was hospitalized on an unspecified day in APR-2022.

At the time of reporting, the event outcome of Chest pain was recovered/resolved and event stop date was 02-MAY-2022. Abdominal pain upper, C-reactive protein increased, Escherichia test positive, Troponin increased, and Urinary tract infection were recovered/resolved.

No additional information is expected.

The 4.1(b) [redacted] narrative was provided as follows:

Central Chest Pain following Novavax Vaccine - hospital admission 27 April 2022. DC summary notes mild troponin rise, assumed to be secondary to UTI From DC summary: 77- year old female who presented to hospital with central chest pain 1. Epigastric pain - ECG NAD - trop rise 175, repeat 302 - CTA unremarkable, troponin rise likely due to UTI described below - Atorvastatin initially increased to 80mg, reduced back to 40mg on discharge Nil changes to medications. Both events /admissions reported here as patient symptoms commenced approx. 2 weeks following different Covid vaccines. Medical Hx: Comorbidities: Hyperlipidaemia, CCF , IHD; Previous MI with previous PCI , CLL , CKD. ADRs: Spironolactone - reduction in renal function; Hydrochlorothiazide - reduction in renal function. Pt admitted to hospital with myopericarditis following Pfizer vax in Nov 2021 - see following - and readmitted to hospital following Novovax in April 2022. Follow up received 17/06/2022 - NSW Health Event notes - Novavax given as D4 April 2022. Admitted to hospital under cardiology team 3 weeks later with central chest pain. Troponin peak 302. CRP 13. ECG NAD. CTA unremarkable, troponin rise likely due to UTI. Urine MCS growth for E coli. Treated with antibiotics. Dx UTI and Epigastric pain. Made phone call with [t. States that she has recovered and as good as she can be considering underlying conditions. 18/05/2022 made phone call patient. States that she has recovered and as good as she can be considering underlying conditions. Reports trusts GP and happy to follow their guidance for future doses. Marked for NSWISS advice to send to GP. ? further vaccine if diagnosed with myo-pericarditis following Pfizer the Novavax. Particularly since clinical diagnosis is that underlying UTI probable cause for troponin rise following Novavax

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				vaccine. PHU to await NSWISS advice then send to GP. On 05-JUL-2022, follow up information was received by Novavax via 4.1(b) reference number: 4.1(b) received the report on 21-JUN-2022. The age of the patient was reported as 77 years (Patient age structured field was left blank as there was a discrepancy of age in the initial (76 years) and follow up (77 years) versions). No new information was received. On 05-JUL-2022, a non-significant correction was made to include the following changes: In the patient tab, other relevant history was corrected to include hyperlipidaemia, congestive cardiac failure, myocardial ischaemia, myocardial infarction, percutaneous coronary intervention, chronic lymphocytic leukaemia, chronic kidney disease, renal impairment with spironolactone, renal impairment with hydrochlorothiazide, and Pfizer Biontech Covid-19 vaccine received in NOV-2021. Lab data was corrected to include Troponin (Result: 175 (no units reported); APR-2022), Troponin (Result: 302 (no units reported); APR-2022), C-reactive protein (Result: 13 (no units reported); APR-2022), Escherichia test (Result: Positive; APR-2022), Electrocardiogram (Result: NAD (no abnormality detected); APR-2022) and Angiogram (Result: Unremarkable; APR-2022).							
4.1(b)	0) 13-APR-22 1) 25-APR-22 2) 08-JUN-22 3) 08-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 17-MAR-2022	Myopericarditis	18-MAR-2022	UNK: 1	Y	Y	Y
		Regulatory Authority	47	1) 0.5 milligram Intramuscular	1) -	Recovered with Sequelae					
			Female				1				
	Case Narrative			On 13-APR-2022, a regulatory authority safety report from 4.1(b) was received by Novavax from a consumer via the 4.1(b)							

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

(Local regulatory reference number: 4.1(b)) via European Medicine Agency (4.1(b) .

A female of an unspecified age was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 17-MAR-2022.

No medical history was reported.

No concomitant medications were reported.

On 18-MAR-2022, 2 days after vaccination, the individual experienced tachycardia (PT: Tachycardia) (Serious: Hospitalization), headache (PT: Headache) (Serious: Hospitalization), vomiting (PT: Vomiting) (Serious: Hospitalization), hypertension (PT: Hypertension) (Serious: Hospitalization), exhaustion (PT: Fatigue) (Serious: Hospitalization), perimyocarditis (PT: Myocarditis) (Serious: Hospitalization and Medically Significant), nausea (PT: Nausea) (Serious: Hospitalization), tiredness (PT: Fatigue) (Serious: Hospitalization) and sleep disturbance (PT: Sleep disorder) (Serious: Hospitalization).

At the time of reporting, the event outcome of Tachycardia was recovered with sequelae and event stop date was 04-APR-2022, Headache was recovered with sequelae and event stop date was 05-APR-2022, Vomiting was recovered with sequelae and event stop date was 05-APR-2022, Hypertension was recovered with sequelae and event stop date was 05-APR-2022, Fatigue was recovered with sequelae and event stop date was 04-APR-2022, Myocarditis was recovered with sequelae and event stop date was 05-APR-2022, Nausea was recovered with sequelae and event stop date was 05-APR-2022, Fatigue was recovered with sequelae and event stop date was 04-APR-2022, and Sleep disorder was recovered with sequelae and event stop date was 04-APR-2022.

Lot number was not provided in the report.

On April 25, 2022, a non significant case correction was identified. Initial Narrative introductory statement should have read: On 04-APR-2022, this initial, serious regulatory authority safety report from 4.1(b) was received from a consumer via the 4.1(b) Local regulatory reference number: 4.1(b)) via European Medicine Agency (4.1(b)) and was received from Novavax on 13-Apr-2022. Additionally amended the adverse events paragraph to include all AEs with the same onset date as per narrative template stated in the

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

data entry manual (DEM).

On 07-JUN-2022, follow up information from 4.1(b) was received from a consumer via 4.1(b) via European Medicines Agency, and was received by Novavax on the 08-June-2022.

The individual reported an age of 47 years, height of 165cm, weight of 47kg, dose/ units of 0.5mL and indication.
The events were described as: 4.1(b). (Headache, vomiting, nausea, high blood pressure. Diagnosis after vaccination: hypertension and perimyocarditis.); and as: 4.1(b). (Tiredness, exhaustion, sleep disorders. High blood pressure, tachycardia. Weakened general condition.)

The regulatory authority's sender comment is as follows:
4.1(b)

(Are you or the affected person aware of allergies? If so, which ones?
No, otherwise no allergies Information on risk factors or previous illnesses No previous illnesses. / 8 hours after administration of the vaccination very severe headache, nausea, vomiting, high blood pressure. After 20 hours by ambulance to the hospital. After 5 days diagnosis of hypertension and perimyocarditis.)

No additional information was provided.

On 01-JUL-2022, a significant case correction with Day 0 of 08-JUN-2022 was identified. The following information was updated: follow-up row 2 received on 08-JUN-2022 significant box checked.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 13-APR-22 1) 08-JUN-22 2) 01-JUL-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 06-MAR-2022	Myopericarditis	07-MAR-2022	UNK: 1	Y	Y	Y
		Regulatory Authority	28	1) 1 dosage form Intramuscular	1) 4301MF009	Not Recovered/Not Resolved					
			Female				1				

Case Narrative

On 14-MAR-2022, this initial, serious regulatory authority safety report from 4.1(b) was received from a consumer via 4.1(b) (Local regulatory reference number: 4.1(b) via European Medicine Agency (Eudravigilance reference number: 4.1(b)), Date of Most Recent Information for this Report was 30-MAR-2022 and was received by Novavax on 13-APR-2022.

An adult female of an unspecified age and race was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 06-MAR-2022.

No medical history was reported.

No concomitant medications were reported.

On 07-MAR-2022, after vaccination, the individual experienced perimyocarditis (PT: Myocarditis) (Serious: Medically Significant).

At the time of reporting, the event outcome of Myocarditis was not recovered/not resolved.

Lot number was not provided in the report.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country / Source	Patient Age Group / Age / Sex	Product Name / Formulation / Dose Details - All	Dose number: Dose Start Date / Batch Numbers	Event Preferred Term / Event Outcome	Event Onset Date / Time To Onset-First dose / Time To Onset-Second Dose / Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
4.1(b)	0) 10-MAY-22 1) 12-MAY-22 2) 25-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 25-MAR-2022	Left ventricular failure	25-MAR-2022	UNK: 0	Y	Y	Y

On 08-JUN-2022, non-significant additional information was received by Novavax from a consumer via the 4.1(b) (Regulatory reference number: 4.1(b)) via the European Medicines Agency (Reference number: 4.1(b) .

The following additional information was provided:
Patient's age (28 years old), Lot number and sender's comment.

The following changes have been made:
There was two identical events (perimyocarditis), therefore the second duplicate event was removed on the event tab. The second duplicate product Nuvaxovid with the same onset date was removed on the products tab.

The regulatory authority's senders comment is as follows:
Pat GC
The diagnosis / suspected diagnosis was supported by the following clarifying examinations:
currently in cardiological co-treatment, findings pending.

No additional information was provided.

On 01-JUL-2022, a significant case correction was identified. The following information was updated: A follow-up line was added to the row 2 in the General tab with a follow up aware date of 01-JUL-2022 and a safety receipt date of 01-JUL-2022.
Upon request the significant box was marked on the first row in the General tab with follow up aware date of 08-JUN-2022.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	3) 08-JUN-22										
		Regulatory Authority	59	1) Intramuscular	1) -	Unknown					
			Male				0				
	0) 10-MAY-22 1) 12-MAY-22 2) 25-MAY-22 3) 08-JUN-22		Adult	NUVAXOVID / Injection	UNK: 25-MAR-2022	Myocarditis	25-MAR-2022	UNK: 0	Y	Y	Y
			59	1) Intramuscular	1) -	Unknown					
			Male				0				

Case Narrative

On 09-MAY-2022, this serious, initial, Regulatory Authority, Safety Report from 4.1(b) was received from a consumer via 4.1(b) (Reference Number: 4.1(b)) and was received by Novavax on 10-MAY-2022 via European Medicines Agency (Reference Number: 4.1(b)).

A male of 59 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose on 25-MAR-2022.

No medical history was reported.

No concomitant medications were reported.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

On 25-MAR-2022, 1 day after vaccination, the individual experienced atrial fibrillation (PT: Atrial fibrillation) (Serious: Hospitalization and Medically Significant).
On 25-MAR-2022, 1 day after vaccination, the individual experienced tingling feet/hands (PT: Paraesthesia) (Serious: Hospitalization).
On 25-MAR-2022, 1 day after vaccination, the individual experienced myocarditis (PT: Myocarditis) (Serious: Hospitalization and Medically Significant).
On 25-MAR-2022, 1 day after vaccination, the individual experienced left ventricular insufficiency (PT: Left ventricular failure) (Serious: Hospitalization and Medically Significant).
On 25-MAR-2022, 1 day after vaccination, the individual experienced light headedness (PT: Dizziness) (Serious: Hospitalization).

At the time of reporting, the event outcome of Atrial fibrillation, Paresthesia , Dizziness, Left ventricular failure and Myocarditis was unknown.

Lot number was not provided in the report.

No additional information is expected.

Verbatim for event lightheadedness updated in the events tab under description as reported to Dizziness as per translation (by ProPharma Group).

On 12-MAY-2022, a non-significant case correction was identified. The following information was updated:
The last sentence of Sender Comment was changed to "is considered as Possible".

On 25-MAY-2022, follow-up information was received by Novavax from a regulatory authority no new information uploaded. Sender's comment was moved from Reporter Comment box to the Sender comment box.

On 07-JUN-2022, follow-up information was received from 4.1(b) from a consumer via 4.1(b) via European Medicines Agency

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				and was received by Novavax on 08-JUN-2022. On 25-MAR-2022, 1 day after vaccination, the individual experienced dilated cardiomyopathy (PT: Congestive cardiomyopathy) (Serious: Hospitalization and Medically Significant). At the time of reporting the event outcome of Congestive cardiomyopathy was unknown.						
4.1(b)	0) 11-MAY-22 1) 18-MAY-22	4.1(b)	Elderly	NUVAXOVID / Injection	3: 23-DEC-2021	Myocarditis	JAN-2022		Y	Y	Y
		Regulatory Authority	65	1) Intramuscular	1) -	Recovered/Resolved					
			Male								

Case Narrative

On 09-MAY-2022, this serious initial regulatory authority safety report from 4.1(b) was received from a physician via the 4.1(b), via the European Medicines Agency 4.1(b) and was received by Novavax on 11-MAY-2022.

A male of 65 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL dose 3 on 23-DEC-2021.

Medical history was reported: Comirnaty (mRNA tozinameran), strength 0.3 mL, with indication prophylactic vaccination administered on 29-APR-2021 and 17-JUN-2021.

No concomitant medications were reported.

On an unspecified day in JAN-2022, after vaccination, the individual experienced acute myocarditis (PT: Myocarditis) (Serious: Hospitalization and Medically Significant).

At the time of reporting, the event outcome of Myocarditis was recovered/resolved.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			The regulatory authority's sender comment is as follows: Echocardiography, coronary angiography Excluded: CHD, stenosis. Lot number was not provided in the report. No additional information was reported. On 18-MAY-2022, a non-significant case correction was identified. The following information was updated: Sender comment was updated as follows: Based on the spontaneous nature of the report, the causal relationship between Nuvaxovid and the reported event is considered possible. No additional information was provided.							
4.1(b)	0) 25-MAY-22 1) 25-MAY-22 2) 08-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 01-APR-2022	Pericarditis	04-APR-2022	UNK: 3	Y	Y	Y
		Regulatory Authority	19	1) 0.5 milliliter Intramuscular	1) 4301MF009	Recovering/Resolving					
			Male				3				

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	0) 25-MAY-22 1) 25-MAY-22 2) 08-JUN-22		Adult	NUVAXOVID / Injection	UNK: 01-APR-2022	Myopericarditis	04-APR-2022	UNK: 3	Y	Y	Y
			19	1) 0.5 milliliter Intramuscular	1) 4301MF009	Recovering/Resolving					
			Male				3				

Case Narrative

On 20-MAY-2022, this serious initial regulatory authority safety report from 4.1(b) was received from a consumer via the 4.1(b)), via the European Medicines Agency 4.1(b) and was received by Novavax on 25-MAY-22.

A male of 19 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on 01-APR-2022.

The following medical history was reported as: Electrocardiogram, Heart rate increased, Pyrexia, Seasonal allergy (to grasses and pollen), Troponin T and Ventricular septal defect.

No concomitant medications were reported.

On 04-APR-2022, 4 days after vaccination, the individual experienced myocarditis (PT: Pericarditis) (Serious: Hospitalization and Medically Significant).

Relevant lab tests included: Echocardiogram (Result: Pericardial thickening up to 8mm in the sense of "adhesion" of the pericardial gap lateral/inferolateral/inferior, compatible with pericarditis. EF 56%, only mildly increased pericardial fluid; 05-APR-2022), Electrocardiogram (Result:

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

Normofrequency, SR (sinus rhythm) , ST (stemi elevations over anterior and posterior wall II, III, aVF, V4-V6; 04-APR-2022), and Electrocardiogram (Result: Slight ascending ST changes over anterior wall, discrete horizontal ST elevation aVF; APR-2022).

At the time of reporting, the event outcome of Pericarditis was recovering/resolving.

No additional information was provided.

The regulatory authority's reporter comment is as follows:
Follow-up of 20-MAY-2022 (doctor's letter of 08-APR-.22): Cardiac echo 05-APR-2022: Pericardial thickening up to 8mm in the sense of "adhesion" of the pericardial gap lateral/inferolateral/inferior, compatible with pericarditis (PT: Pericarditis) (Serious: Hospitalization and Medically Significant). EF (ejection faction) 56%, only mildly increased pericardial fluid. Cardio MRI (magnetic resonance imaging) was refused by the patient. ECG (Electrocardiogram) 04-APR-2022: normofrequency, SR (sinus rhythm) , ST (stemi elevations over anterior and posterior wall II, III, aVF, V4-V6. ECG at discharge: slight ascending ST changes over anterior wall, discrete horizontal ST elevation aVF. BC Level 1 (Troponin I AND pericardial wall thickness change).

A regulatory authority's sender comment is as follows: Non-intervention-required VSD, 3mm / thoracic tightness, subfebrile temperature, high heart rate up to 130'/min, ECG changes in the sense of (peri-) myocarditis, Troponin T up to 34000 pg/ml. Currently beta-blocker therapy and NSAIDs with proton pump inhibitors. 6 months sports ban.

On 27-MAY-2022, a significant case correction with Day 0 of 25-MAY-2022 was identified. The following information was updated: event description as reported - myocarditis was updated to Plus especially myocarditis (not verifiable, because MRI rejected by the patient).

On 08-JUN-2022, follow-up information was received by Novavax from a consumer, via 4.1(b) [redacted]) via the European Medicines Agency 4.1(b) [redacted]).

The following information was updated in the case:
On 04-APR-2022, four days after vaccination, the individual experienced Perimyocarditis (Plus especially myocarditis (not verifiable, because MRI

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

rejected by the patient)) (PT: Myopericarditis)(Serious: Hospitalization and Medically Significant).
At the time of reporting, the event outcome of Myopericarditis was recovering/resolving.

The following changes have been made:
The second duplicate product Nuvaxovid with the same start date and Batch number was removed from the product's tab. For the event Pericarditis(PT: Pericarditis), the description as reported 'Plus especially myocarditis (not verifiable, because MRI rejected by the patient)' was changed to 'Pericarditis'.

The previous regulatory authority's sender comment is as follows :
Are you or the affected person aware of allergies? If so, which ones? Grasses and pollen Information on risk factors or pre-existing conditions. Non-intervention-required VSD, 3mm / thoracic tightness, subfebrile temperature, high heart rate up to 130'/min, ECG changes in the sense of (peri-) myocarditis Are you or the affected person aware of allergies? If so, which ones? Grasses and pollen Information on risk factors or pre-existing conditions Troponin T up to 34000 pg/ml. Currently beta-blocker therapy and NSAIDs with proton pump inhibitors. 6 months sports ban.

No additional information was provided.

4.1(b)	0) 06-JUN-22 1) 07-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 19-MAR-2022	Red blood cell sedimentation rate increased			N	Y	Y
		Regulatory Authority	60	1) 0.5 milliliter Intramuscular	1) 4301MF009	Unknown					
			Female								

Case Narrative

On 25-MAY-2022 this non-serious initial regulatory authority safety report from 4.1(b) was received from a physician by the 4.1(b) (reference number: 4.1(b)) via the European Medicines Agency (4.1(b)) and was received by Novavax on 06-JUN-2022.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

A female of 60 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL unspecified primary dose on 19-MAR-2022.

The following medical history was reported: Allergy to metals and Myalgia.

No concomitant medications were reported.

On 02-MAR-2022, after vaccination, the individual experienced fatigue (PT: Fatigue), feeling of weakness both legs (PT: Muscular weakness), and muscle pain both arms (PT: Myalgia). On an unspecified date, after vaccination, the individual experienced increased blood values leukos (PT: Leukocytosis), increased blood values CRP (PT: C-reactive protein increased), and increased blood values ESR (PT: Red blood cell sedimentation rate increased).

The following relevant treatment was reported: Painkillers ibuprofen, novaminsulfone, prednisolone, 10 days antibiotics administration.

At the time of reporting, the event outcomes of Muscular weakness, Fatigue, and Myalgia were not recovered/not resolved, and Red blood cell sedimentation rate increased, C-reactive protein increased, and Leukocytosis were unknown.

The regulatory authority's narrative was provided as follows:
Are you or the affected person aware of allergies? If so, which ones?
Nickel allergy
Information on risk factors or pre-existing conditions
No pre-existing conditions. No medication. Until now, painkillers for acute muscle pain. / Date of birth4.1(b) 1961 Since exacerbation of the symptoms after 2 vaccination. Painkillers ibuprofen, novaminsulfone, prednisolone . Blood sampling in which high leukos, ESR and CRP values were detected. Because of suspicion of bakt. Infection 10 days antibiotics administration. After that, unfortunately, even higher CRP and ESR values.

On 07-JUN-2022 a non-significant case correction was identified. The following information was updated: Initial paragraph updated about reporter

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			type from physician to consumer. On 25-MAY-2022 this non-serious initial regulatory authority safety report from 4.1(b) was received from a consumer by the 4.1(b) (reference number: 4.1(b)) via the European Medicines Agency 4.1(b) and was received by Novavax on 06-JUN-2022. The description as reported of the following events were reverted to originally imported values in foreign language : 4.1(b) . (Feeling of weakness both legs. Pain in feet) (PT: fatigue), 4.1(b) (constant cramps thighs, feet, thickening muscle strands back of the knee, increased blood values leukos, CRP, ESR, neutrophils, after 10 days of antibiotics administration even higher. Muscle pain both arms) (PT: Myalgia).						
4.1(b)	0) 27-JUN-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 07-MAR-2022	Myocarditis	17-JUN-2022	UNK: 102	Y	Y	Y
		Regulatory Authority	44	1) 1 dosage form Intramuscular	1) 430MF009	Unknown					
			Male				102				

Case Narrative

On 24-JUN-2022, this serious initial regulatory authority safety report from 4.1(b) was received from a consumer via the 4.1(b) Regulatory Agency 4.1(b) (4.1(b)), via the European Medicines Agency (4.1(b) and was received by Novavax on 27-JUN-2022.

A male of 44 years was vaccinated with an unspecified primary dose number of intramuscular Nuvaxovid 10 ug/mL (1 dosage form) on 07-MAR-2022.

No medical history was reported.
No concomitant medications were reported.

On 17-JUN-2022, 3 months 11 days after vaccination, the individual experienced myocarditis (PT: Myocarditis) (Serious: Hospitalization and

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			Medically Significant). On an unspecified date, after vaccination, the individual experienced exertional dyspnea (PT: Dyspnoea exertional) (Serious: Hospitalization), intercostal neuralgia (PT: Intercostal neuralgia) (Serious: Hospitalization) and chest ache (Chest pain) (PT: Chest pain) (Serious: Hospitalization). At the time of reporting, the event outcomes of Chest pain, Myocarditis, Intercostal neuralgia and Dyspnoea exertional were unknown.							
4.1(b)	0) 13-APR-22 1) 28-APR-22 2) 03-MAY-22 3) 17-MAY-22 4) 31-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 01-APR-2022	Ventricular extrasystoles	01-APR-2022	UNK: 0	Y	Y	Y
		Regulatory Authority	40	1) Intramuscular	1) 4301MF009	Unknown					
			Female								
							0				
Case Narrative			On 01-APR-2021 this serious, initial regulatory authority safety report from 4.1(b) was received by Novavax on 13-APR-2022 from an other health professional via 4.1(b) (reference # 4.1(b) and European Medicines Agency (reference # 4.1(b) . A female of an unspecified age was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose on 01-APR-2022. No medical history was reported.								

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)

The following concomitant medications were reported: cetirizine hydrochloride taken oral for Allergy prophylaxis.

On 01-APR-2022, the individual experienced sleepiness (PT: Somnolence) (Serious: Hospitalization).
On 01-APR-2022, the individual experienced heart rate increased (PT: Heart rate increased) (Serious: Hospitalization).
On 01-APR-2022, the individual experienced revaccination with different covid-19 vaccine (PT: COVID-19 immunisation) (Serious: Hospitalization).
On 01-APR-2022, the individual experienced tremor (PT: Tremor) (Serious: Hospitalization).
On 01-APR-2022, the individual experienced fatigue (PT: Fatigue) (Serious: Hospitalization).
On 01-APR-2022, the individual experienced lip oedema (PT: Lip oedema) (Serious: Hospitalization).
On 01-APR-2022, the individual experienced malaise (PT: Malaise) (Serious: Hospitalization).

At the time of reporting, the event outcome of Tremor, Somnolence, Heart rate increased, COVID-19 immunisation, Malaise, Fatigue and Lip oedema was unknown.

LOT/Batch number was not provided.

On 28-APR-2022, follow-up information was received by Novavax from an other health professional. The other health professional reported the following information:

The female individual was 41 years at the time of reaction/event onset.

On 01-APR-2022, the individual experienced sinus tachycardia (PT: Sinus tachycardia) (Serious: Hospitalization), vaccination site pain (PT: Vaccination site pain) (Serious: Hospitalization), allergic reaction NOS (PT: Hypersensitivity) (Serious: Hospitalization), ventricular extra systoles (PT: Ventricular extra systoles) (Serious: Hospitalization), feeling abnormal (PT: Feeling abnormal) (Serious: Hospitalization), loss of consciousness (PT: Loss of consciousness) (Serious: Hospitalization and Medically Significant), dyspnoea (PT: Dyspnoea) (Serious: Hospitalization), pharynx discomfort (PT: Oropharyngeal discomfort) (Serious: Hospitalization), lower extremities weakness of (PT: Muscular weakness) (Serious: Hospitalization), leukocyte count increased (PT: White blood cell count increased) (Serious: Hospitalization), toothache (PT:

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

Toothache) (Serious: Hospitalization), erythema facial (PT: Erythema) (Serious: Hospitalization), blood pressure increased (PT: Blood pressure increased) (Serious: Hospitalization), vaccination site lump (PT: Vaccination site mass) (Serious: Hospitalization).

At the time of reporting follow-up, the event outcome of Vaccination site pain, Hypersensitivity, Ventricular extra systoles, Feeling abnormal, Loss of consciousness, Dyspnoea, Oropharyngeal discomfort, Muscular weakness, White blood cell count increased, Toothache, Erythema, Blood pressure increased, Vaccination site mass, and Sinus tachycardia were unknown.

On 03-MAY-2022 significant follow-up information was received by Novavax. The following information was reported: Concomitant medication was added: Tamofen [tamoxifen citrate].

Based on internal review on 17-May-2022, a non-significant case correction was thought to have been identified and was subsequently retracted with the receipt of additional information received on 31-MAY-2022. The two document were processed together and it was identified that no further action was needed.

During the processing of the above case corrections the following corrections were also implemented: An additional reporter was identified as a physician, reported on 28-APR-2022, this had not been commented upon in the narrative, and is now here described; the events of PT: Somnolence and PT: Fatigue were doubled - the duplicate events were deleted; the patient age was deleted due to the age being reported as both 40 years and 41 years, on 28-APR-2022. The suspected dose was reported on 28-APR-2022 as Dose 3, this was captured but not commented upon in the narrative, and is now here described. The concomitant cetirizine administered was reported as Histec (10mg once daily, oral, stat dose on 01-APR-2022), on 28-APR-2022, this was captured but not commented upon in the narrative, and is now here described. These appeared to represent non-significant changes.

On 31-MAY-2022, a non-significant case correction was identified. The following information was updated:
The age of the patient in the Patient tab was updated to 40 years of age as included in a statement on source document FUP2.1.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
4.1(b)	0) 28-APR-22 1) 03-MAY-22 2) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 07-APR-2022	Supraventricular tachycardia	07-APR-2022	UNK: 0	N	Y	Y
		Regulatory Authority	44	1) Intramuscular	1) -	Recovered/Resolved					
			Female				0				

Case Narrative

On 18-Apr-2022, this initial, non-serious regulatory authority safety report from 4.1(b) was received from a consumer via the 4.1(b)), via the European Medicine Agency (4.1(b) and was received by Novavax on 28-Apr-2022.

A female of 44 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose on 07-APR-2022.

No medical history was reported.
No concomitant medications were reported.

On 07-APR-2022, 1 dayafter vaccination, the individual experienced asthenia (PT: Asthenia).
On 07-APR-2022, 1 dayafter vaccination, the individual experienced vaccination site pain (PT: Vaccination site pain).
On 07-APR-2022, 1 dayafter vaccination, the individual experienced myalgia (PT: Myalgia).
On 07-APR-2022, 1 dayafter vaccination, the individual experienced tachycardia (PT: Tachycardia).

At the time of reporting, the event outcome of Asthenia was recovered/resolved, Tachycardia was recovered/resolved, Myalgia was recovered/resolved and Vaccination site pain was recovered/resolved.

Lot number was not provided in the report.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				Based on internal review on 17-MAY-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from assessed as possible to was considered possible. The sender comment location was moved from the reporter comment field to the sender comment field.							
4.1(b)	0) 06-MAY-22 1) 11-MAY-22	4.1(b) Regulatory Authority	Elderly 65 Female	NUVAXOVID / Injection 1) Intramuscular 2) Intramuscular	1: 04-MAR-2022 2: 26-MAR-2022 1) - 2) -	Pericarditis Recovering/Resolving	27-MAR-2022 23 1 1	1: 23 2: 1	Y	Y	Y

Case Narrative

On 26-APR-2022, this serious, initial spontaneous regulatory authority safety report from 4.1(b) was received from a physician via the 4.1(b) Regulatory Agency 4.1(b)), via the European Medicine Agency (4.1(b)) and was received by Novavax on 06-MAY-2022.

A female of 65 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 04-MAR-2022 and primary dose 2 on 26-MAR-2022.

The following medical history was reported: Pulmonary arterial hypertension, Syndrome sicca and Systemic sclerosis.

No concomitant medications were reported.

On 27-MAR-2022, 24 days after vaccination, the individual experienced pericarditis (PT: Pericarditis) (Serious: Hospitalization and Medically Significant).

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			At the time of reporting, the event outcome of Pericarditis was recovering/resolving. Lot number was not provided in the report. On 12-MAY-2022, a non-significant case correction was identified. The following information was updated: The last sentence of Sender Comment was changed to "is considered as Possible".								
4.1(b)	0) 13-APR-22 1) 03-MAY-22 2) 04-MAY-22 3) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 10-MAR-2022 16:39:00	Electrocardiogram abnormal	18-MAR-2022	UNK: 7.3	Y	Y	Y
		Regulatory Authority	37	1) 0.5 milliliter Intramuscular	1) 4301MF011	Recovering/Resolving					
			Male				7.3				
Case Narrative			On 13-APR-2022, a serious initial regulatory authority safety report from 4.1(b) was received by Novavax from a consumer via EMA (European Medicine Agency) (Eudravigilance reference number 4.1(b)). A male of an unspecified age was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose on 10-MAR-2022. No medical history was reported. No concomitant medications were reported.								

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

On 18-MAR-2022, 9 daysafter vaccination, the individual experienced brugada-type ecg (Serious: Life-Threatening).
On 18-MAR-2022, 9 daysafter vaccination, the individual experienced arrhythmia (PT: Arrhythmia) (Serious: Life-Threatening and Medically Significant).
On 18-MAR-2022, 9 daysafter vaccination, the individual experienced chest ache (PT: Chest pain) (Serious: Life-Threatening).

At the time of reporting, the event outcome of arrhythmia was not recovered/not resolved, electrocardiogram abnormal was not recovered/not resolved and chest pain was not recovered/not resolved.

Lot number was not provided in the report.

On 03-May-2022, additional information was received from a consumer via the 4.1(b) (reference number; 4.1(b) and the following information were updated - patient age as 37, body weight 64 kg, height- 169 cm, lot number-4301MF011, dose - 0.5 milliliters.

The regulatory authority events and reporter's comment is as follows(translated by PPG);
Action/events as reported by primary source; It was reported that a week after receiving the covid novavax vaccine the individual went to hospital with strong burning in his chest and back and blood pressure of 150/100 a non-brugada syndrome arrhythmia pattern is detected.

Allergic history; It was also reported that the individual was allergic to diphtheria-tetanus vaccine

The regulatory authority sender's comments is as follows (translated by PPG); 1st dose of Nuvaxovid vaccine on 10/MAR/2022 at 16:39 hours in left deltoid, lot number 4301MF011, expiry date 31/AUG/2022

No additional information was reported.

On 04-May-2022, additional information was received from a consumer via the 4.1(b) Regulatory Authority (reference number; 4.1(b)

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

4.1(b)) and the following information was updated as outcome of all events from not recovered/ not resolved to recovering/resolving. No additional information was reported.

Based on internal review on 17-MAY-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from 'were assessed as related' to 'is considered possible'. The sender comment location was moved from the 'reporter comment field' to the 'sender comment field.'

4.1(b)	0) 13-APR-22 1) 29-APR-22 2) 17-MAY-22	4.1(b)	Adult	NUVAXOVID / Injection	UNK: 14-MAR-2022	Extrasystoles	14-MAR-2022	UNK: 0	N	Y	Y
		Regulatory Authority	58	1) 1 dosage form Intramuscular	1) 4301MF011	Not Recovered/Not Resolved					
			Male				0				

Case Narrative

On 25-MAR-2022, a non-serious initial regulatory authority safety report from 4.1(b) was received from a consumer via other (Local regulatory reference number: 4.1(b) and European Medicines Agency 4.1(b) , Date of most recent information for this report was 01-APR-2022 and was received by Novavax on 13-APR-2022

A male of an unspecified age and race was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 14-MAR-2022.

No medical history was reported.

No concomitant medications were reported.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				

On 14-MAR-2022, after vaccination, the individual experienced deglutition disorder (PT: Dysphagia), extrasystoles (PT: Extrasystoles), felt faint (PT: Dizziness), tachycardia (PT: Tachycardia), sense of oppression (PT: Sense of oppression), tinnitus (PT: Tinnitus), nausea (PT: Nausea), and hypertension (PT: Hypertension).

At the time of reporting, the event outcome of Dysphagia, Tinnitus, Tachycardia, Nausea, Extrasystoles, Dizziness, Hypertension, and Sense of oppression was not recovered/not resolved.

Lot number was not provided in the report.

No additional information was provided.

On 29-APR-2022, a significant follow-up information was received by Novavax from a patient/consumer via European Medicines Agency (reference number: 4.1(b) [redacted]). The following information was updated in the case: Adverse event description as reported provided in original language 4.1(b) for all events. Relevant lab tests were reported: Blood pressure (156/107 international unit(s)-(under 1000)), Heart rate (129 international unit(s)-(under 1000)). Patient age of 58 years, weight and height were reported. Vaccination batch number, dosage of 1 dosage form.

No additional information was provided.

On 24-MAY-2022, a non-significant case correction was identified. The following information was updated: translation for source document was added and updates to the sender comment. The regulatory authority's sender comment is as follows:

RLF: further information required (specialist reports) 25/03/2021. CRFV 29/03/2022 Requests / solicitations information for clinical evolution, pathologies and therapies
concomitants and clinical report. Updated field SM susp, severity, instrumental and laboratory tests and feedback from the reporter with removal of sensitive data. RLF: other reports pending 01/04 / 2022.CRFV updated field adverse reaction instrumental tests.

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
	Based on internal review on 17-MAY-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The sender comment location was moved from the reporter comment field to the sender comment field. The causality was updated from "were assessed as related" to "was considered possible".										
4.1(b)	0) 13-APR-22 1) 17-MAY-22	4.1(b)		NUVAXOVID / Injection	UNK: 28-FEB-2022	Extrasystoles	08-MAR-2022	UNK: 8	N	Y	Y
		Regulatory Authority	Unknown	1) 0.5 milliliter Parenteral	1) -	Not Recovered/Not Resolved					
			Male				8				

Case Narrative

This serious initial regulatory authority safety report from 4.1(b) was received by Novavax on 13-APR-2022 from a consumer via European Medicine Agency (reference 4.1(b)).http://4.1(b)

A male of an unspecified age was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose on 28-FEB-2022.

No medical history was reported.

No concomitant medications were reported.

On 08-MAR-2022, 9 days after vaccination, the individual experienced extrasystoles (PT: Extrasystoles), armpit pain (PT: Axillary pain), axillary pain (PT: Axillary pain), blood pressure increased (PT: Blood pressure increased), exhaustion (PT: Fatigue), pain chest (PT: Chest pain), arrhythmia (PT: Arrhythmia) (Serious: Medically Significant).

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				At the time of reporting, the event outcomes of Extrasystoles, Axillary pain, Arrhythmia, Fatigue, Chest pain, and Blood pressure increased were not recovered/not resolved. Lot number was not provided in the report. Based on internal review on 17-May-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made: The causality was updated from were assessed as related to were considered possible The sender comment location was moved from the reporter comment field to the sender comment field.						
4.1(b)	4.1(b)	4.1(b	Adult	NUVAXOVID / Injection	UNK: 15-APR-2022	Pericarditis	18-APR-2022	UNK: 3	Y	Y	Y
		Regulatory Authority	47	1) 1 dosage form Intramuscular	1) 4301MF011	Not Recovered/Not Resolved					
			Female				3				
Case Narrative				On 03-JUN-2022, this serious initial regulatory authority safety report from 4.1(was received from a consumer via the 4.1(b) Regulatory Authority 4.1(b)) via the European Medicines Agency (4.1(b) and was received by Novavax on 06-JUN-2022. A female of 47 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 15-APR-2022. The following medical history was reported: Anemia, Hepatitis B surface antigen, Thrombocytopenia and Uterine leiomyoma. The following concomitant medications were reported: Tranex (tranexamic acid). On 18-APR-2022, 4 daysafter vaccination, the individual experienced 4.1(b) (Marked allergic skin reaction) (PT: Skin						

COVID-19 VACCINE Cumulative until 30-Jun-2022

Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country Source	Patient Age Group Age Sex	Product Name / Formulation Dose Details - All	Dose number: Dose Start Date Batch Numbers	Event Preferred Term Event Outcome	Event Onset Date Time To Onset-First dose Time To Onset-Second Dose Time to Onset-Last Dose	Time to Onset - All Doses	Ser	Causal	UL (CORE)
				Reaction), 4.1(b) (increased blood pressure) (PT: Blood Pressure increase) 4.1(b) (appearance of herpetic labial) (PT: Oral herpes) 4.1(b) (cardiac alterations from acute pericarditis) (PT: Pericarditis). At the time of reporting, the event outcomes of Skin reaction, Pericarditis, Blood pressure increased and Oral herpes were not recovered/not resolved. The regulatory authority's sender comment is as follows: As reported by the reporter: - other relevant medical information: HBSAG positive, anaemia, fibromatous uterus, recurrent thrombocytopenia episodes. The regulatory authority's reporter comment is as follows: Other drugs or products taken at the same time: potassium ascorbate with ribose that I have been taking for many years, iron and Tranex as needed that I have been taking for a long time without ever having had any reaction				
4.1(b)	0) 09-JUN-22 1) 13-JUN-22	4.1(b) Regulatory Authority	Adult 44 Male	NUVAXOVID / Injection 1) 0.5 milliliter Intramuscular	UNK: 28-FEB-2022 1) 4301MF011	Extrasystoles Not Recovered/Not Resolved	08-MAR-2022 8	UNK: 8	N	Y	Y
	Case Narrative			On 07-JUN-2022, an initial, serious regulatory safety report from 4.1(was received from the 4.1(b) Medicines Agency 4.1(b) via the European Medicines Agency 4.1(b)) and was received by Novavax on 09-JUN-2022. A male of 44 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose on 28-FEB-2022 in an unspecified location. The following medical history was reported: Mite allergy and Seasonal allergy.							

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				No concomitant medications were reported. On 08-MAR-2022, 9 daysafter vaccination, the individual experienced 4.1(b) [redacted] pain and heat in the sub-axillary lymphatic tracts) (PT: Axillary pain). On 08-MAR-2022, 9 daysafter vaccination, the individual experienced 4.1(b) [redacted] (Lack of strength, heat in the back, heat and sensation of nail in the chest, arrhythmias in extrasystole,) (PT: Arrhythmia) (Serious: Medically Significant). On 08-MAR-2022, 9 daysafter vaccination, the individual experienced 4.1(b) [redacted] (Lack of strength, heat in the back, heat and sensation of nail in the chest, arrhythmias in extrasystole) (PT: Extrasystoles). At the time of reporting, the event outcome of Axillary pain was not recovered/not resolved, Extrasystoles was not recovered/not resolved and Arrhythmia was not recovered/not resolved. No additional information is expected. The regulatory authority's reporter comment translated is as follows: Allergies to mites and pollen. Symptoms of arrhythmia extrasystolar are still present. On 13-JUN-2022, a non-significant case correction was identified. The following information was updated: The original language for each event was changed from English and the sender comment from "The event Arrhythmia was reported as serious." to "The event Arrhythmia was assessed as serious." to reflect that the event was upgraded to serious based on the IME list.							
4.1(b) [redacted]	0) 13-APR-22 1) 17-MAY-22	4.1(b) [redacted]	Adult	NUVAXOVID / Injection	1: 01-MAR-2022	Extrasystoles	MAR-2022		N	Y	Y
		Regulatory	Unknown	1) Intramuscular	1) -	Not					

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Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
		Authority				Recovered/Not Resolved					
			Female								

Case Narrative

On 13-APR-2022, a regulatory authority report from 4.1(b) was received from a consumer via Regional pharmacovigilance centre (4.1(b))and was received by Novavax on 13-APR-2022.

A female of an unspecified age was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 01-MAR-2022.

The following medical history was reported: Polyneuropathy chronic, an unspecified medical condition (since 2005), and an unspecified past drug (given on 08-AUG-2021).

The following concomitant medications were reported: Lyrica (pregabalin) given orally (since 2021).

On 01-MAR-2022, reported to be the day of vaccination, the individual experienced revaccination with different covid-19 vaccine (PT: COVID-19 immunisation).
On an unspecified day in MAR-2022, after vaccination, the individual experienced headache (PT: Headache) and extrasystoles (PT: Extrasystoles).

At the time of reporting, the event outcomes of Headache and Extrasystoles were not recovered/not resolved. COVID-19 immunisation was recovered/resolved and event stop date was 01-MAR-2022.

No additional information expected.

Based on internal review on 17-MAY-2022, a non-significant case correction was identified. The following updates to the Sender Comment were made:
The causality was updated from 'were assessed as possible' to 'is considered as possible'. The sender comment location was moved from the

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
			reporter comment field to the sender comment field.								
4.1(b)	0) 13-APR-22 1) 13-APR-22	4.1(b)	Adult	NUVAXOVID / Injection	3: 31-MAR-2022	Pericarditis	01-APR-2022 14:41:00	3: 1.6	Y	Y	Y
		Regulatory Authority	28	1) Intramuscular	1) -	Not Recovered/Not Resolved					
			Female				1.6				

Case Narrative

On 06-APR-2022, this initial, serious Regulatory Authority safety report from 4.1(b) was received from a consumer via 4.1(b) (4.1(b) reference number: 4.1(b)) and was received by Novavax on 13-APR-2022.

A female of 28 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL with primary dose 3 on 31-MAR-2022.

The following medical history was reported: Pfizer BioNtech Covid-19 Vaccine (Dose-1) and Covid-19 vaccine AstraZeneca (Dose-2).

No concomitant medications were reported.

On 01-APR-2022 at 14:41, after third dose of vaccination, the individual initially felt chest pressure and discomfort (PT: Chest discomfort) for a few days until it changed to chest pain on the 04-APR-2022. The individual went to the hospital and was diagnosed with pericarditis (PT: Pericarditis) (Serious: Medically Significant). On 01-APR-2022 at 14:41, after third dose of vaccination, the individual also experienced fatigue (PT: Fatigue) and headache (PT: Headache). The individual also received emergency care.

At the time of reporting, the event outcomes of Chest discomfort, Fatigue, Headache and Pericarditis were not recovered/not resolved.

Lot number was not provided in the report.

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Myocarditis and Pericarditis CIOMS II LL Cumulative

Case Number	Case Receipt Dates	Country	Patient Age Group	Product Name / Formulation	Dose number: Dose Start Date	Event Preferred Term	Event Onset Date	Time to Onset - All Doses	Ser	Causal	UL (CORE)
		Source	Age	Dose Details - All	Batch Numbers	Event Outcome	Time To Onset-First dose				
			Sex				Time To Onset-Second Dose				
							Time to Onset-Last Dose				
				No additional information was provided. On 15-APR-2022, a significant case correction with Day 0 of 13-APR-2022 was identified. The following information was updated: Seriousness criteria of Hospitalization was added for events of Pericarditis, Chest discomfort and Fatigue and the narrative was amended accordingly. For event of chest discomfort, the additional verbatim " initially felt chest pressure and discomfort for a few days until it changed to chest pain" was removed from the description as reported field. In the second paragraph of the narrative, "primary" dose was removed since the patient received Nuvaxovid as a 3rd dose.							

Total Row Count: 85
Total Case Count: 68

Appendix

Section Title	Template Name	Query Name	Criteria
Myocarditis and Pericarditis CIOMS II LL Cumulative	CIOMS II Line Listing with Batch# and Narrative	Event criteria for Special topics with case validity	(((Event Preferred Term =) OR (Event High Level Term = Infectious myocarditis OR Event High Level Term = Noninfectious myocarditis OR Event High Level Term = Infectious pericarditis OR Event High Level Term = Noninfectious pericarditis) OR (Event High Level Group Term =) OR (Event System Organ Class =) OR (Event SMQ (Broad) = Noninfectious myocarditis/pericarditis (SMQ)) OR (Event SMQ (Narrow) =)) AND ((Case Validity = Valid) OR (Case Validity Is null)))

Appendix 22: Signal Evaluation Report of Paraesthesia

SAFETY SIGNAL EVALUATION REPORT FOR

Paraesthesia with Use of COVID-19 Vaccine (Recombinant, Adjuvanted) (NVX-COV2373)

Main Brand Names: NUVAXOVID™

Date of Report: 07-JUL-2022

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Marketing Authorization Holder:

(NOVAVAX, Inc.)

Electronic signature approval(s) signifies that the approver approves this document as acceptable, accurate, and complete.

DESCRIPTION	NAME / TITLE	SIGNATURE / DATE
PREPARED BY:	4.1(b)	4.1(b)
APPROVED BY:	4.1(b)	
APPROVED BY:	4.1(b)	

Executive Summary

Nuvaxovid/Covid-19 Vaccine (recombinant, adjuvanted) (NVX-CoV2373) is indicated for active immunization to prevent Coronavirus Disease-19 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals aged 18 years of age and older (authorised as Covovax in India and Thailand for ages > 12 and < 18 years).

Nuvaxovid is a purified full-length SARS-CoV-2 recombinant spike (S) protein that is stabilised in its prefusion conformation. The addition of the saponin-based Matrix-M™ adjuvant facilitates activation of the cells of the innate immune system, which enhances the magnitude of the S protein-specific immune response. The 2 vaccine components elicit B- and T-cell immune responses to the S protein, including neutralising antibodies, which may contribute to protection against COVID-19.

A signal of Paraesthesia and Hypoaesthesia was validated following the European Medicines Agency (EMA) request for more information which was included in the Assessment Report for Safety Summary Report (SSR) # 03 dated on 27-May-2022. Additionally, a request was received from the Therapeutic Goods Administration (TGA) on 01-Jun-2022 to add Paraesthesia and Hypoaesthesia to the reference safety information (RSI) in Australian Nuvaxovid Label. The request was to update the Product Information section 4.8 (Adverse Effects) language to include paraesthesia and hypoaesthesia.

The safety database (Argus) was queried for cumulative Individual Case Safety Report (ICSRs) using the prespecified Medical Dictionary for Regulatory Activities (MedDRA) search strategy of High Level Term (HLT): Paraesthesias and dysaesthesias. Cumulatively, there were 244 ICSRs identified for Paraesthesias through 31-May-2022.

A case series analysis was performed on all ICSRs retrieved by looking at Preferred Term(s) (PTs) retrieved from HLT: Paraesthesias and dysaesthesias search strategy and also grouping the ICSRs based on their co-reported PTs to evaluate for any patterns and to understand the clinical picture in occurrence of Paraesthesias. Over 80% of ICSRs are reported form Australia and Germany. Paraesthesia has been reported in 79% females. The most commonly co-reported PTs with Paraesthesia were headache (27%), fatigue (26%), dizziness (23%),

chest pain (21%), pain in extremity (17%), injection site pain (16%), nausea (15%), myalgia (13%), pyrexia (12%), and chest discomfort (10%). Most of the Paraesthesia events following vaccination were generally mild and transient. Time to onset was between 0 to 5 days. There were no documented any specific treatments for the Paraesthesia. Outcome was reported as not resolved in most reports, and 2 reports indicated outcome of resolved with sequelae. It is early in the Post-authorization experience with Nuvaxovid (no reports were received before 21-Feb-2022) and it is therefore difficult to draw conclusions with the current data. However, long-term sequelae are unlikely. None of the cases had a fatal outcome. After detailed review of all ICSRs, no potential etiological factors or trends were identified.

Worldwide Market Authorization Status

On 20-Dec-2021, the first marketing authorization (MA) for Nuvaxovid was granted in European Union which is considered to be the International Birthdate (IBD).

Source of Signal

Paresthesia has been a safety observation since meeting the EudraVigilance Data Analysis System (EVDAS) Electronic Reaction Monitoring Report (eRMR) criteria for the period of 01 through 15-MAR-2022 (n=5 reports, ROR of 3.58). The most recent eRMR (16-May-2022 through 31-MAY-2022) indicated an n=94 and ROR of 5.79 with a change status of "increasing".

The signal of Paraesthesia was identified for validation following an European Medicines Agency (EMA) request for more information included in the PRAC Assessment Report for Safety Summary Report (SSR) # 03 dated on 27-May-2022. Additionally, a request was received from the TGA on 01-Jun-2022 to add Paraesthesia and Hypoaesthesia to the reference safety information in Australian Nuvaxovid Label.

Objective

The objective of this report is to describe a comprehensive review of the safety data relevant to Paraesthesias from all available sources to determine whether the available evidence supports or refutes an association between Nuvaxovid and Paraesthesias.

Cumulative Clinical Exposure Data

Clinical Trial Integrated Safety Summary: N=30075 in the active (NVX-CoV2373) arm and N=19875 in the placebo arm.

A pooled analysis of safety data was performed. This integrated safety summary (ISS) evaluated data pertaining to adult participants that were exposed to NVX-CoV2373 from the start of first vaccination through the data extraction dates of the respective clinical studies including 28 July 2021 for 2019nCoV-101 Part1, 11 June 2021 for 2019nCoV-101 Part2, 10 September 2021 for2019nCoV-302, 23 February 2021 for /2019nCoV-501and 17 September 2021 for 2019nCoV-301 was evaluated for unsolicited adverse events reported from Day 0 to Day 49 (28 Days post Dose 2). An updated ISS with extraction dates of the respective clinical studies of 28 July 2021 for 2019nCoV-101 Part1, 11 June 2021 for 2019nCoV-101 Part2, 04 October 2021 for2019nCoV-302, 27 October 2021 for /2019nCoV-501and 20 January 2022 for 2019nCoV-301 was evaluated for the serious adverse events, pre and post crossover, and for the PT of Paraesthesia and Hypoaesthisa utilizing the SMQ of Peripheral Neuropathy.

Post-marketing Exposure Data

Cumulatively up to the cut off date of 31 May 2022, 942,554 Nuvaxovid doses were administered in Australia, Canada, EU, Japan, New Zealand, and South Korea and a total of 46,640,860 NVX-CoV2373 doses (37,432,860 NUVAXOVID and 9,208,000 Covovax doses) were distributed globally.

Methods

Clinical Trial data included ISS data: 28 July 2021 for 2019nCoV-101 Part1, 11 June 2021 for 2019nCoV-101 Part2, 10 September 2021 for2019nCoV-302, 23 February 2021 for 2019nCoV-501and 17 September 2021 for 2019nCoV-301 and updated ISS data 28 July 2021 for 2019nCoV-101 Part1, 11 June 2021 for 2019nCoV-101 Part2, 04 October 2021 for2019nCoV-302, 27 October 2021 for /2019nCoV-501and 20 January 2022 for 2019nCoV-301). Clinical data was reviewed for the PTs of Paraesthesias and Hypoaesthesia. Additionally, the ISS was searched for PT containing “esthesia” to ensure every Paraesthesia was captured and its frequency compared to placebo group.

Post-authorization data included the Argus safety databasewas queried for cumulative ICSRs using the prespecified search strategy of HLT: Paraesthesias and dysaesthesias up to 31 May 2022. Cumulatively, there were 244 ICSRs identified for the search strategy for Paraesthesia.. A case series analysis was performed on all ICSRs and grouping the ICSRs based on their co-reported PTs to evaluate for any patterns and to understand the clinical picture in occurrence of Paraesthesias.

Disproportionality statistics: EVDAS eRMR results were evaluated for signals of disprportionate reporting (ROR>1; n ≥ 3) **Results**

Clinical Trial data was reviewed by using the ISS from 2019nCoV-101 Part1, 2019nCoV-101 Part2, 2019nCoV-501, 2019nCoV-302, 2019nCoV-301. Injection site hypoaesthesia was infrequent and balanced, occurring in 10 (0.03%) and 3 (0.02%) of NVX-CoV2373 and placebo recipients, respectively. Injection site paraesthesia and vaccination site paraesthesia was less frequent and also balanced, occurring in 3 (<0.01%) and 1 (<0.01%) and 1 (<0.1%) and 2 (0.01%) of NVX-CoV2373 and placebo recipients, respectively. Paraesethesia occurred with a greater frequency in the placebo group, reported in 29 (0.10%) of NVX-CoV2373 recipients and 27 (0.14%) placebo recipients. Hypoaesthesia was balanced, occurring in 17 (0.06%) and 11 (0.06%) of NVX-CoV2373 and placebo recipients, respectively.

An updated ISS was utilized to evaluate the occurrence of serious adverse events with the PT of Paraesthesia or Hypoaesthesia. No serious adverse events were reported in the pre-crossover or post-crossover periods.

The updated ISS was also utilized to evaluate the incidence rate (IR) per 100 person years for PTs of Paraesthesia and Hypoaesthesia captured using the Broad Standardized MedDRA Query (SMQ) for Peripheral Neuropathy from Day 0 to EOS and also within 3 days post vaccination. From Day 0 to End of follow up, the IR of paraesthesia was greater in the placebo group; 31 events with an IR of 0.42 e/100 Patient Years (PY) in the active group vs 28 events with an IR of 0.57 e/100 PY in the placebo group. The IR of hypoasthesia was the same in the active and placebo group, 0.27 e/100 PY. Using the same Broad SMQ, the IR of paraesthesia was also greater in the placebo group within 3 days of vaccination, 16 events IR of 0.21 e/100 PY in the active group and 16 events IR of 0.33 e/100 PY in the placebo group. The results for hypoaesthesia noted 7 events IR of 0.09 e/100PY in the active group and 5 events IR of 0.10 e/100 PY in the placebo group.

Post -authorization data was reviewed as of the data cut of 31-May-2022. Cumulatively, a total of 244 spontaneous ICSRs were retrieved from the safety database that met the search criteria. A case series analysis was performed on all ICSRs retrieved by looking at PTs retrieved from HLT: Paraesthesias and dysaesthesias search strategy and grouping the ICSRs based on their co-reported PTs to evaluate for any patterns and to understand the clinical picture in the occurrence of Paraesthesias. Over 80% of ICSRs are reported form Australia and Germany and 79% of the ICSRs were reported in females. The most commonly co-reported events with Paraesthesias were headache (27%), fatigue (26%), dizziness (23%), chest pain (21%), pain in extremity (17%), injection site pain (16%), nausea (15%), myalgia (13%), pyrexia (12%), and chest discomfort (10%). Most of the Paraesthesias events following vaccination were generally mild and transient. Time to onset was between 0 to 5 days. There were no documented treatments for the Paraesthesias. Outcome was reported as

not resolved in most reports, and 2 reports indicated outcome of resolved with sequelae. It is early in the post-authorization experience with Nuvaxovid (no reports were received before 21-Feb-2022) and it is therefore difficult to draw conclusions with the current data, however, long-term sequelae are unlikely. None of the cases had a fatal outcome. After detailed review of all ICSRs, no potential etiological factors or trends were identified.

Paresthesia has been a safety observation since meeting the EVDAS eRMR criteria for the period of 01 through 15-MAR-2022 (n=5 reports, ROR = 3.58). The most recent eRMR (16-May-2022 through 31-MAY-2022) indicated an n=94 and ROR of 5.79 with a change status of “increasing”.

Conclusion

The signal is confirmed based on a comprehensive review of the available evidence that does support a causal association between Nuvaxovid use and Paraesthesia.

Safety Review Team Signal Disposition

- The Australian label section 4.8 (Adverse Effects) will be updated as requested. A labeling variation was submitted.
- Routine monitoring is recommended without updates to the CCDS.

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LIST OF ABBREVIATIONS

Acronym	Abbreviation Definition
AESI	Adverse Events of Special Interest
CCDS	Company Core Data Sheet
CI	Confidence Interval
COVID	Coronavirus Disease
DLP	Data Lock Point
EMA	European Medicines Agency
eRMR	Electronic Reaction Monitoring Report
EU	European Union
EUA	Emergency Use Authorization
EVDAS	EudraVigilance Data Analysis System
HLT	High Level Term
IBD	International Birth Date
ICSR	Individual Case Safety Report(s)
ISS	Integrated Safety Summary
MA	Marketing Authorization
MAH	Marketing Authorization Holder
MedDRA	Medical Dictionary for Regulatory Activities
N/A	Not Applicable / Not Available
NVX	Novavax, Inc.
O/E	Observed versus Expected
PT	Preferred Term(s)
PVA	Pharmacovigilance Agreements

Acronym	Abbreviation Definition
PY	Patient Years
RA	Regulatory Authority(s)
ROR	Reporting Odds Ratio
rSARS-CoV-2 SPG	Recombinant Severe Acute Respiratory Coronavirus 2 Spike Glycoprotein
RSI	Reference Safety Information
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SDR	Signals of Disproportionate Reporting
SIIPL	Serum Institute of India Pvt. Ltd
SMQ	Standardized MedDRA Query
SOC	System Organ Classes
SSR	Summary Safety Report
TGA	Therapeutic Goods Administration
TTO	Time to Onset
UK	United Kingdome
US/USA	United States of America
UAE	United Arab Emirates
v	Version
WHO	World Health Organisation

1 INTRODUCTION

This signal evaluation report provides a detailed analysis on the validated safety signal of Paraesthesia in association with the administration of Nuvaxovid indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older (authorised as Covovax in India and Thailand for ages > 12 and < 18 years).

Nuvaxovid is a purified full-length SARS-CoV-2 recombinant spike (S) protein that is stabilised in its prefusion conformation. The addition of the saponin-based Matrix-M™ adjuvant facilitates activation of the cells of the innate immune system, which enhances the magnitude of the S protein-specific immune response. The 2 vaccine components elicit B- and T-cell immune responses to the S protein, including neutralising antibodies, which may contribute to protection against COVID-19. Further details on the mechanism of action, indications, pharmaceutical form(s), and instructions for use are presented in the Nuvaxovid Reference Safety Information (RSI) in effect during the beginning of reporting interval was the Company Core Data Sheet (CCDS) Version (V) 3.0 effective date 03-May-2022.

2 WORLDWIDE MARKET AUTHORIZATION STATUS

On 20-Dec-2022, the first marketing authorization (MA) for Nuvaxovid was granted in European Union which is considered to the be International Birthdate (IBD).

Nuvaxovid and Covovax have been granted authorisation(s) in the countries and regions in the table below. To fulfill Pharmacovigilance (PV) requirements by country/regional regulatory authorities (RA), NVX has entered into Pharmacovigilance Agreements (PVAs) with Biocelect (Australia, New Zealand), SK Bioscience (South Korea), PharmEng Technology Pte Ltd. (Singapore), Future Health Pharma GmbH (Switzerland), Takeda (Japan), and Serum Institute of India Pvt. Ltd. (SIIPL; Indonesia, Philippines, World Health Organisation [WHO], and India, Bangladesh, and Thailand).

Country	Authorisation Type	Authorisation / Approval Date	Partner Name / MAH
Indonesia	EUA[a]	31-Oct-2021	SIIPL
Philippines	EUA[a]	17-Nov-2021	SIIPL
WHO	EUL[a]	17-Dec-2021	SIIPL
WHO	EUL[b]	20-Dec-2021	NVX CZ
EU	CMA[b]	20-Dec-2021	NVX CZ
UAE	EUA[b]	26-Dec-2021	GULF MED MEDICINES L.L.C.
India	EUA[a]	28-Dec-2021	SIIPL

	Adult ≥ 18 years		
India	EUA[a] Adolescents ≥ 12 to < 18 years	09-Mar-2022	SIIPL
South Korea	BLA[b]	12-Jan-2022	SK Bioscience Co., Ltd.
Australia	Provisional Registration[b]	20-Jan-2022	Biocelect Pty Ltd.
UK	CMA[b]	03-Feb-2022	NVX CZ
Singapore	Interim Authorisation (PSAR)[b]	03-Feb-2022	PharmEng Technology Pte Ltd.
New Zealand	Provisional Consent[b]	04-Feb-2022	Biocelect New Zealand Ltd.
Canada	NDS[b]	17-Feb-2022	NVX Inc
Bangladesh	EUA[b]	22-Feb-2022	SIIPL
Thailand	EUA[a]	22-Mar-2022	SIIPL
Switzerland	CMA[b]	12-Apr-2022	Future Health Pharma GmbH
Japan	J-NDA[b]	19-Apr-2022	Takeda
Thailand	EUA[a] Adolescents ≥12 to <18 yrs	11-May-2022	SIIPL

[a] COVOVAX

[b] NUVAXOVID

Abbreviations: BLA: Biologics License Application; CMA: Conditional Marketing Authorisation; CZ EU: European Union; EUA: Emergency Use Authorisation; EUL: Emergency Use Listing; NDS: New Drug Submission; NVX CZ: Novavax Czech Republic Ltd.; PSAR: Pandemic Special Access Route; SIIPL: Serum Institute of India Pvt. Ltd.; UAE: United Arab Emirates; UK: United Kingdom; WHO: World Health Organisation, J-NDA-Japan New Drug Application.

3 SOURCE OF THE SIGNAL

Paresthesia has been a safety observation since meeting the EVDAS eRMR criteria (ROR>1; n≥3) for the period of 01 through 15-MAR-2022 (n=5 reports, ROR = 3.58). The most recent eRMR (16-May-2022 through 31-MAY-2022) indicated an n=94 and ROR of 5.79 with a change status of “increasing” for the MedDRA Preferred Term Paraesthesia and an n=35 and ROR of 2.62 with a change status of “increasing” for the MedDRA Preferred Term Hypoaesthesia.

A signal of Paraesthesia and Hypoaesthesia was validated following the EMA request for more information which was included in the PRAC Assessment report for Safety Summary Report (SSR) No.03 dated on 27-May-2022. Additionally, a request was received from the TGA on 01-Jun-2022 to add Paraesthesia and Hypoaesthesia to the RSI in Australian Nuvaxovid Label. The request was to update the Product Information section 4.8 (Adverse Effects) language to include paraesthesia and hypoaesthesia.

4 BACKGROUND

4.1 Background Related to Paraesthesia

Paresthesia is characterized by functional disturbances of sensory neurons resulting in abnormal cutaneous sensations of tingling, numbness, pressure, cold, and/or warmth.[1] It is also described as a burning or prickling sensation that is usually felt in the hands, arms, legs, or feet, but can also occur in other parts of the body. The sensation, which happens without warning, is usually painless and described as tingling or numbness, skin crawling, or itching.[2]

Transient paresthesia is commonly due to inadvertent nerve compression on an arm or leg. Several diseases are characterized by paresthesia as an initial symptom. These include central and peripheral nervous system disorders, metabolic disorders, toxins, infections, rheumatologic disorders, and cancer and cancer-related disorders.[3] Paresthesia has been reported after vaccination with Nuvaxovid and other COVID-19 vaccines. In a nationwide descriptive study of adverse events after vaccination with BNT162b2 mRNA COVID-19 in Mexico, transient sensory symptoms (paresthesia, dysesthesia, numbness, pinprick, tingling, or a combination thereof) were among the most frequently reported non-serious neurologic complaints. The study found a disproportionate number of neurologic events in female recipients, which the authors attributed in part to sexual dimorphism of the immune system.[4]

For Nuvaxovid, Nervous System Disorders is the second most common MedDRA System Organ Classes (SOC) represented in the adverse events. The HLT of Paraesthesias and dysaesthesias is the largest HLT represented in the Nervous System Disorders SOC, accounting for 4.1% of all reported events and 21% of the reported events in the MedDRA SOC of Nervous System Disorders. Paraesthesia has consistently been among the top 20 reported events each week since March 2022. Paraesthesias has been a safety observation since meeting the EVDAS eRMR criteria for the period of 01 through 15-MAR-2022 (n=5 reports, ROR = 3.58). The most recent eRMR (16 May2022 through 31-MAY-2022) indicated an n=94 and ROR of 5.79 with a change status of “increasing”.

5 EXPOSURE DATA

5.1 Cumulative Subject Exposure in Clinical Trials

Clinical Trial: N=30075 in the active (NVX-CoV2373) arm and N=19875 in Placebo arm.

5.2 Cumulative Exposure Data from Post-Marketing Experience

Post-marketing: during the reporting interval, 192,908 NUVAXOVID doses were administered in Australia, Canada, EU, Japan, New Zealand, and South Korea and a total of 1,567,860 NVX-CoV2373 doses (1,567,860 Nuvaxovid and 0 Covovax doses) were distributed globally. Cumulatively, 942,554 Nuvaxovid doses were administered in Australia, Canada, EU, Japan, New Zealand, and South Korea and a total of 46,640,860 NVX-CoV2373 doses (37,432,860 Nuvaxovid and 9,208,000 Covovax doses) were distributed globally.

6 METHODS

6.1 Search Strategy

6.1.1 Clinical Studies

Clinical Trial data included ISS data: 28 July 2021 for 2019nCoV-101 Part1, 11 June 2021 for 2019nCoV-101 Part2, 10 September 2021 for2019nCoV-302, 23 February 2021 for 2019nCoV-501and 17 September 2021 for 2019nCoV-301 and updated ISS data 28 July 2021 for 2019nCoV-101 Part1, 11 June 2021 for 2019nCoV-101 Part2, 04 October 2021 for2019nCoV-302, 27 October 2021 for /2019nCoV-501and 20 January 2022 for 2019nCoV-301). Clinical data was reviewed for the PTs of Paraesthesias and Hypoaesthesia. Additionally, the ISS was searched for PT containing “esthesia” to ensure every Paraesthesia was captured and its frequency compared to placebo group.

6.1.2 Post-marketing Safety Database

Safety Data from Argus included a cumulative search with MedDRA search strategy of the HLT: Paraesthesias and dysaesthesias with a data lock point (DLP) of 31-May-2022.

All ICSRs have been reviewed and categorized based on the co-reported terms, to ascertain the constellation of symptoms which may represent potential etiological factors. The cases are presented by the co-reported terms categories, in a cascading manner. Some cases may appear in more than one table when multiple co-reported terms do not seem to fit into one category. The last table in the series contains cases which have not yet been discussed in the report and do not fit in any prior table.

Disproportionality statistics included reviewing the EVDAS eRMR criteria for the period of 16 -May-2022 through 31-MAY-2022.

6.2 Analysis Strategy

Case Definition

All Post-marketing ICSRs that contained PTs from the search criteria of HLT: Paraesthesias and dysaesthesias through 31-May-2022. Additionally, all Post-marketing ICSRs were medically reviewed and categorized based on the co-reported terms, to ascertain the constellation of symptoms which may represent potential etiological factors.

6.3 Disproportionality Statistics

Disproportionality statistics from EVDAS: MedDRA PT: Paraesthesias became a signal of disproportionate reporting (SDR) based on EVDAS eRMR (16-May-2022 to 31-Mar-2022; n=94, ROR=5.79) with a change status of "increasing" and an n=35 and ROR of 2.62 with a change status of "increasing" for the MedDRA Preferred Term Hypoaesthesia.
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7 RESULTS

7.1 Analysis of Data from Clinical Studies

The data received from clinical studies (28 July 2021 for 2019nCoV-101 Part1, 11 June 2021 for 2019nCoV-101 Part2, 04 October 2021 for2019nCoV-302, 27 October 2021 for /2019nCoV-501and 20 January 2022 for 2019nCoV-301) showed that there was no difference in the frequency of occurrence between PTs of Paraesthesias and Hypoaesthesias in active group treated with NVX-CoV2373 as compared to placebo group.

Clinical Trial data was reviewed by using the ISS from 2019nCoV-101 Part1, 2019nCoV-101 Part2, 2019nCoV-501, 2019nCoV-302, 2019nCoV-301. Injection site hypoaesthesia was infrequent and balanced, occurring in 10 (0.03%) and 3 (0.02%) of NVX-CoV2373 and placebo recipients, respectively. Injection site paraesthesia and vaccination site paraesthesia was less frequent and also balanced, occurring in 3 (<0.01%) and 1 (<0.01%) and 1 (<0.1%) and 2 (0.01%) of NVX-CoV2373 and placebo recipients, respectively. Paraesthesia occurred with a greater frequency in the placebo group, reported in 29 (0.10%) of NVX-CoV2373 recipients and 27 (0.14%) placebo recipients. Hypoaesthesia was balanced, occurring in 17 (0.06%) and 11 (0.06%) of NVX-CoV2373 and placebo recipients, respectively.

An updated ISS was utilized to evaluate the occurrence of serious adverse events with the PT of Paraesthesia or Hypoaesthesia. No serious adverse events were reported in the pre-crossover or post-crossover periods.

The updated ISS was also utilized to evaluate the incidence rate (IR) per 100 person years for PTs of Paraesthesia and Hypoaesthesia captured using the Broad Standardized MedDRA Query (SMQ) for Peripheral Neuropathy from Day 0 to EOS and also within 3 days post vaccination. From Day 0 to End of follow up, the IR of paraesthesia was greater in the placebo group; 31 events with an IR of 0.42 e/100 PY in the active group vs 28 events with an IR of 0.57 e/100 PY in the placebo group. The IR of hypoasthesia was the same in the active and placebo group, 0.27 e/100 PY. Using the same Broad SMQ, the IR of paraesthesia was also greater in the placebo group within 3 days of vaccination, 16 events IR of 0.21 e/100 PY in the active group and 16 events IR of 0.33 e/100 PY in the placebo group. The results for hypoaesthesia noted 7 events IR of 0.09 e/100PY in the active group and 5 events IR of 0.10 e/100 PY in the placebo group.

Additional relevant clinical study data is summarized in Table 1 , Table 2 and Table 3.

Table 1: Summary of Retrieved Events from Clinical Studies Summary of Event Rates of Adverse Events by Peripheral Neuropathy (SMQ) Reported During the Study (from Day 0 to End of follow-up)

MedDRA (v23.0) SMQ Broad SMQ for Peripheral Neuropathy **Preferred Term**	**Population**	
	Vaccine (N=30058) n, rate per 100 person-years 95% CI	**Placebo (N=19892) n, rate per 100 person-years, 95%CI**
Nervous system disorders	54 (0.72), (0.54, 0.94)	45 (0.92), (0.67, 1.23)
Paraesthesia	31 (0.42)	28 (0.57)
Hypoaesthesia	20 (0.27)	13 (0.27)

Table 2: Summary of Retrieved Events from Clinical Studies Summary of Event Rates of Adverse Events by Peripheral Neuropathy (SMQ) Reported During the Study within 3 Days Post Vaccination

MedDRA (v23.0) SMQ Broad SMQ for Peripheral Neuropathy **Preferred Term**	**Population**	
	Vaccine (N=30058) n, rate per 100 person-years, 95%CI	**Placebo (N=19892) n, rate per 100 person-years, 95%CI**
Nervous system disorders	25 (0.33), (0.22, 0.49)	22 (0.45), (0.28, 0.68)
Paraesthesia	16 (0.21)	16 (0.33)
Hypoaesthesia	7 (0.09)	5 (0.10)

Table 3: Summary of Retrieved Events from Clinical Studies Summary of Unsolicited Adverse Events Reported from Day 0 to 49 (28 Days Post Dose 2)

MedDRA (v23.0) Preferred Term	Population	
	Vaccine (N=30075) n (%)	Placebo (N=19875) n (%)
Injection site hypoaesthesia	10 (0.03)	3 (0.02)
Injection site paraesthesia	3 (<0.01)	1 (<0.01)
Vaccination site paraesthesia	1 (<0.01)	2 (0.01)
Paraesthesia	29 (0.10)	27 (0.14)
Hypoaesthesia	17 (0.06)	11 (0.06)
Hyperaesthesia	2 (<0.01)	0 (0.00)
Paraesthesia oral	4 (0.01)	0 (0.00)
Pharyngeal hypoaesthesia	1 (<0.01)	0 (0.00)
Paraesthesia ear	1 (<0.01)	0 (0.00)
Genital paraesthesia	1 (<0.01)	0 (0.00)
Hemiparaesthesia	1 (0.01)	0 (0.00)
Hyperaesthesia teeth	0 (0.00)	1 (<0.01)
Hypoaesthesia oral	0 (0.00)	1 (<0.01)

7.2 Analysis of ICSRs from Post-market Safety Database

Cumulatively, there were 244 ICSRs identified for the search strategy for Paraesthesia from HLT: Paraesthesias and dysaesthesias through 31-May-2022. A case series analysis was performed on all ICSRs retrieved by looking at PTs retrieved from HLT:

Paraesthesias and dysaesthesias search strategy and grouping the ICSRs based on their co-reported PTs to evaluate for any patterns and to understand the clinical picture in occurrence of Paraesthesias.

Demographics (n=244)

Figure 1: Post Market ICSRs Age and Sex Distribution

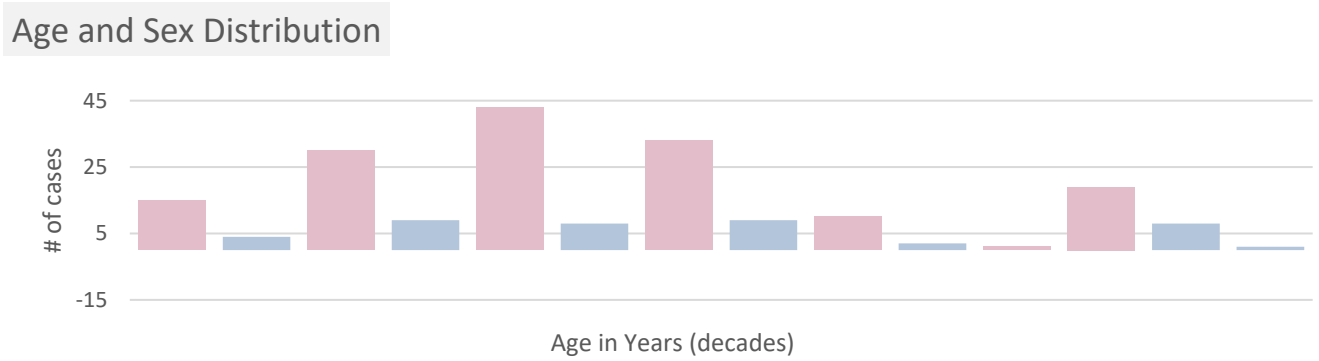


Figure 2: Post Market ICSRs Countries

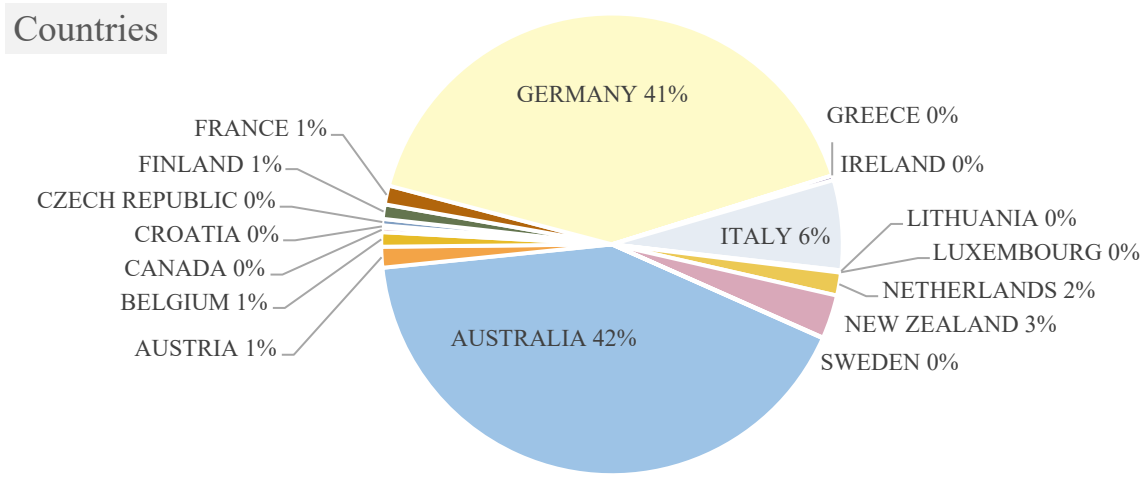
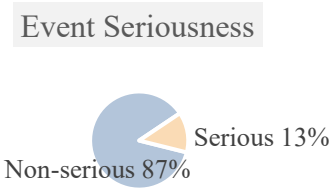


Figure 3: Post Market ICSRs % of Seriousness criteria



ICSR Analysis (n=244)

The following PTs were represented in the data for HLT of Paraesthesias and Dysaesthesias:

Twenty-two (22) cases involved a single PT of Paraesthesia with no co-reported events, 4 cases involved a single PT of Hypoasethesia with no co-reported events, and 1 case involved a single PT of Burning sensation with no co-reported events. The remaining 217 cases involved one or more co-reported events. The most commonly co-reported were headache (27%), fatigue (26%), dizziness (23%), chest pain (21%), pain in extremity (17%), injection site pain (16%), nausea (15%), myalgia (13%), pyrexia (12%), and chest discomfort (10%). The majority of cases have been received from Health Authorities thus ICSR generally reflect outcomes at the time of initial ICSR reporting.

Table 4: PT Categorization of Retrieved ICSR

MedDRA PT (v25.0)	N
Paraesthesia	199
Hypoaesthesia	67
Burning sensation	22
Hyperaesthesia	6
Dysaesthesia	5
Hemiparaesthesia	2
Total Events	301

Table 5: Report Characteristics

Total ICSRs*	244

		n	%
Report Origin	Australia	133	54.5
	Germany	78	32.0
	Italy	16	6.6
	New Zealand	11	4.5
	France	3	1.2
	Austria	1	0.4
	Canada	1	0.4
	Finland	1	0.4
Seriousness criteria	Serious n=28	28	11
	• Hospitalization	8	29
	• Fatal	0	0
	Non-serious n=216	216	89
MedDRA terms	Paraesthesia	189	77
	Hypoaesthesia	64	26
	Burning sensation	22	9
	Hyperaesthesia	6	2
	Dysaesthesia	5	2
	Hemiparaesthesia	2	1
Event latency (n=43)	0- 5 days	41	95
	6-10 days	2	5
	Over 10 days	0	0
Event treatment (n=6)	Ibuprofen	3	50
	Homeopathic care	1	17
	Vitamin C	1	17
	Prednisolone, Electrolytes, Aspirin	1	17

Event outcome (n=244)	Not Recovered/Not Resolved	156	64
	Recovering/Resolving	33	14
	Recovered/Resolved	26	11
	Recovered with Sequelae	2	1
	Unknown	28	11

Figure 4: Post Market ICSRs Outcome

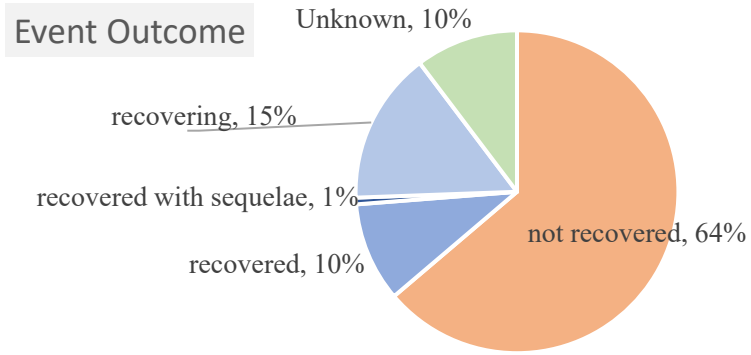


Table 6: **Summary Table of No Co-Reported Events or Minimal similar Co-reported Events**

Presented in the table below are the cases with the event of interest alone or with minimal co-reported terms. These cases have either just the events of interest (in the HLT Paraesthesias and dysaesthesias), and/or one additional co-reported term of pain in extremity, vaccination site pain, feeling cold, nervous system disorder, pain, or paraesthesia oral. The events are sorted by Event Outcome. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information such as concomitant medications and relevant/ descriptive details, is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)	4.1(b)	43M	Same day	Not resolved	Unknown	Skin discomfort, Hyperaesthesia	Not Reported	Skin in the body sensitive to touch, as if the lower layer of the skin is inflamed
		44F	< 3 weeks (est)	Not resolved	2 months (est)	Nervous system disorder, Paraesthesia	Not reported	
		50F	3 weeks (est)	Not resolved	43 days	Paraesthesia	Not reported	
		45F	<1 week (est)	Not resolved	55 days	Paraesthesia	Not reported	
		29F	<2 weeks (est)	Not resolved	46 days	Burning sensation	Not reported	
		81F	<2 weeks (est)	Not resolved	44 days	Paraesthesia, Pain	Not reported	
		34M	<2 weeks (est)	Not resolved	43 days	Paraesthesia	Not reported	
		50F	<1 week (est)	Not resolved	Unknown	Paraesthesia	Not reported	
		Unk M	<3 weeks (est)	Not resolved	Unknown	Paraesthesia Pain in extremity	Not reported	
		62F	< 4 weeks (est)	Not resolved	2 months (est)	Paraesthesia	Not reported	
		41M	< 2 weeks (est)	Not resolved	3 months (est)	Paraesthesia	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		45F	(estimate) 3 months	Not resolved	2 days	Paraesthesia	Not reported	
		57F	Unknown	Not resolved	3 months (est)	Hypoaesthesia	Not reported	
		31F	Unknown	Not resolved	3 months (est)	Paraesthesia Pain in extremity	Not reported	
		53M	Unknown	Not resolved	3 months (est)	Paraesthesia	Not reported	
		53F	11 days	Not resolved	74 days	Paraesthesia	Not reported	
		Unk F	1 day	Not resolved	74 days	Paraesthesia, Paraesthesia	Not reported	Paresthesia, Paraesthesia lower limb
		Unk F	2 months	Not resolved	74 days	Paraesthesia	Not reported	Comirnaty was reported as a secondary suspect.
		Unk F	1 day	Not resolved	74 days	Paraesthesia	Not reported	Comirnaty was reported as a secondary suspect.
		52F	1 day	Not resolved	72 days	Hypoaesthesia Paraesthesia	Allergy to grass, rye, pollen;	Directly when vaccinating tingling in the upper left arm and left thumb, since

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
							Hashimoto's thyroiditis, Hypoaesthesia	then numbness in left thumb, still 20 days after vaccination.
4.1(b)		26F	Within 15 minutes	Not resolved	Unknown	Hypoaesthesia Paraesthesia	Mite allergy Seasonal allergy	Numbness in the fingers and a tingling during the 15-minute waiting period after vaccination.
		23F	2 days	Not resolved	3 weeks	Paraesthesia	Not reported	1 month pregnant at vaccination. Very strong numbness for 4 days, 2 weeks after vaccination miscarriage, 3 weeks later mild numbness still present without further improvement.
		66F	4 days	Not resolved	Unknown	Paraesthesia, Vaccination site pain	Hypertension, Osteoarthritis	Tingling of extremity
		Unk F	2 days	Not resolved	Unknown	Paraesthesia, Pain in extremity	Not reported	Tingling feet/hands
		54F	3 days	Not resolved	52 days	Sensory disturbance, Paraesthesia, Paraesthesia, Neuralgia	Not reported	Pins and needles
		40M	Same day	Ongoing	18 days	Neuropathy peripheral,	Not reported	peripheral neuropathy - pins and needles, mild nerves pain on the left leg.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
medically confirmed						Neuralgia, Paraesthesia		Treatment administered by pharmacist but not reported. No previous vaccine reactions.
4.1(b)		27F	2 days	Ongoing	81 days	Paraesthesia, Paradoxical drug reaction	Not reported	Numbness of the whole skull; Numbness of left leg 2 days after vaccination.
		42F	Same day	Resolved	50 days	Paraesthesia	Not reported	
		39F	< 3 weeks (est)	Resolved	< 2 weeks (est)	Hypoaesthesia, Paraesthesia, Pain	Not reported	
		55F	1 day	Resolved	59 days	Paraesthesia Hypoaesthesia Hypoaesthesia Dysaesthesia	Not reported	Tingling of extremity, Buttock numbness, Hypoesthesia, Dysaesthesia of lower extremity
		55F	same day	Resolved	1 day	Paraesthesia	Not reported	
		Unk F	Unknown	Resolved	< 3 months	Paraesthesia, Injection site pain	Allergy to arthropod sting and food	Tingling in the fingers

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		55F	0 days	Resolved	1 day	Paraesthesia	Not reported	
		40F	<11 weeks (est)	Resolved	15 days	Pruritus, Paraesthesia	Not reported	
		45F	Same day	Resolving	43 days, resolving	Paraesthesia Feeling cold	Not reported	Slight tingling of lips and cheeks and freezing on the day of the vaccination. 10 minutes later, the tingling has calmed down. 30 minutes later, mild tingling still present. Freezing cold resolved on the same day.
		52F	Day 0	Resolving	60 days	Paraesthesia	Not reported	6 hours after vaccination, the individual experienced tingling in the toes of both feet
		37F	10 days	Resolving	11 days	Paraesthesia	Allergy to arthropod bite	Tingling on the right palm (vaccinated on left)
		30F	2 days	Resolving	4 weeks, recovering	Hypoaesthesia	Neurodermatitis, Food allergy	Numbness of half of body (leg, arm, face), massive in the first week, then temporary wavelike course. 4 weeks after vaccination still occurs sporadically, but only in

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								individual regions of the body.
4.1(b)		34M	0 days	Resolving	Unknown	Paraesthesia	Not reported	
		Unk M	1 day	Resolving	34 days, resolving	Paraesthesia, Paraesthesia oral	Not reported	Tingling lips, feet, and hands.
		Unk F	<1week (est)	Unknown	48 days	Hypoaesthesia	Not reported	
		47F	2 months(est)	Unknown	Unknown	Hypoaesthesia	Not reported	
		Unk F	1 day	Unknown	78 days, unknown	Paraesthesia	Not reported	Facial paresthesia
		33M	3 days 21 hrs	Unknown	Unknown	Paraesthesia	NA	

Abbreviations: Refer to Abbreviations Table

Forty-four (44) ICSRs included the event of interest alone or in combination with minimum other co-reported terms. The majority (76%) were females ranging in age from 23 years to 81 years. Time to onset was reported in 25 cases, with 12 reports having a zero to one day time to onset, and the remaining reports 2 days to < 2 weeks. Concomitant medications were not reported in any of the reports. There were 4 reports among females with reported medical history, which was largely allergic in nature. In one report [redacted]) an individual underwent various examinations which could not identify any other etiologies or triggers.

Table 7: Summary Table of Co-Reported Events with Narrow SMQ of Hypersensitivity

Presented in the table below are the cases with the event of interest, co-reported with terms belonging to the Narrow SMQ of Hypersensitivity. The events are sorted by Event Outcome. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information such as concomitant medications and relevant/descriptive details, is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		35F	<2 weeks (est)	Not resolved	2 months	Anaphylactic reaction, Hot flush, Dyspnoea, Paraesthesia, Dyspnoea exertional, Dizziness, Hyperhidrosis, Lethargy, Hypersensitivity	Rheumatoid arthritis, GERD	Paraesthesia – tingling on the arm
		55F	1 day	Not resolved	6 days	Feeling hot, Lip discoloration, Palpitations, Paraesthesia, Rash erythematous, Thirst, Pruritus	Not reported	
		55F	<2 weeks (est)	Not resolved	2 months	Chest discomfort, Cough, Cyanosis, Dermatitis, Dyspnoea, Feeling hot, Inflammation, Paraesthesia, Injection site pain	Not reported	
		56F	<1 week (est)	Not resolved	1 week	Dyspnoea, Chest pain, Diarrhoea, Hypoaesthesia, Palpitations, Paraesthesia, Tachycardia, Vision blurred, Rash, Pain in extremity, Pyrexia	Not reported	Other reported PT: shivering (tremor). Tests: right arm doppler, elevated ESR, LDH, GGT, ALT and D-dimer.
		25F	<1 month (est)	Not resolved	1 month	Dizziness, Hyperhidrosis, Paraesthesia, Swelling,	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Swelling face, Hyperventilation, Pain in extremity, Hypersensitivity, Fatigue, Nausea		
4.1(b)		34M	18 hours	Not resolved	1 month	Eye swelling, Nausea, Chest pain, Concomitant disease aggravated, Ear congestion, Feeling hot, Palpitations, Paraesthesia, Fatigue	Not reported	Felt fatigued, nausea and chest issues within 3 hours of vaccination. Visited the hospital within 7 hours of vaccination.
		51F	Unknown	Not resolved	2 months (est)	Lip swelling, Eye swelling, Vision blurred, Dizziness, Muscular weakness, Hypoaesthesia, Paraesthesia,	Not reported	Con meds: Vitamin C and D, Valtrex,Quercetain, Panadolosteo, Lyrica, Docusate, Fish oil,Spiractin, Magnesium, Choline bitartrate,Endep, K2, Doxycycline, Fess, Patanol, Celebrex, Metformin, Loratadine, Iron, Pantoprazole, Famotidine, Voltaren.
		44F	40 days (est)	Not resolved	43 days	Swelling face, Vomiting, Chest discomfort, Breast	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						pain, Chest pain, Confusional state, Diarrhoea, Discolored vomit, Exercise tolerance decreased, Faeces pale, Lethargy, Migraine, Urinary tract infection, Injection site reaction, Paraesthesia		
4.1(b)		27F	57 days (est)	Not resolved	60 days	Rash macular, Erythema, Chest discomfort, Chest pain, Dyspnoea, Lymphadenitis, Influenza like illness, Lymphadenopathy, Pruritus, Arthralgia, Injection site pain, Burning sensation	Not reported	
		46F	Unknown	Not Resolved	2 months ongoing (est)	Musculoskeletal stiffness, Dizziness, Paraesthesia, Rash macular, Injection site pruritus, Headache, Fatigue, Injection site pain	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		65F	Unknown	Not Resolved	1 1/2 months (est)	Rash pruritic, Erythema, Burning sensation,	Not reported	
		Unk F	Unknown	Not Resolved	2 months (est)	Rash, Pyrexia, Chest pain, Dyspnoea, Lethargy, Migraine, Myalgia, Paraesthesia	Not reported	
		Unk F	Same day	Not resolved	75 days	Rash, Paraesthesia	Not reported	
		33F	1 day	Not resolved	73 days	Rash, Hemiparaesthesia, Palpitations	Not reported	1 day after vaccination, the individual experienced heart racing, hemiparaesthesia and skin rash. Con meds: Not reported
		Unk F	1 day	Not resolved	Unknown	Swelling face, Peripheral swelling, Oedema peripheral, Pain in extremity, Dry mouth, Myalgia, Malaise, Arthralgia, Fatigue, Noninfective gingivitis, Paraesthesia	Not reported	Tingling sensation
		47F	0 day	Not resolved	10 days	Rash, Heart rate irregular, Injection site pain, Hypoaesthesia	Not reported	Numbness
		37F	same day	Not Resolved	Unknown	Face oedema, Abdominal pain,	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Chest discomfort, Diarrhoea, Dizziness, Insomnia, Oropharyngeal pain, Palpitations, Photophobia, Influenza like illness, Lymphadenopathy, Injection site pain, Fatigue, Headache, Pyrexia, Myalgia, Nausea, Hypoaesthesia		
4.1(b)		32F	<4 weeks (est)	Ongoing	7 days	Hypersensitivity, Alopecia, Dizziness, Eye pain, Memory impairment, Tinnitus, Headache, Vomiting, Paraesthesia	Not reported	
		40M	< 4 weeks (est)	Resolved	< 4 weeks (est)	Rash, Paraesthesia	Not reported	
		43M	< 4 weeks (est)	Resolved	< 1 weeks (est)	Anaphylactic reaction, Tachycardia, Vision blurred, Chest pain, Paraesthesia, Tremor, headache	Not reported	

		Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		42F	0 day	Resolved	<1 day	Circulatory collapse, Feeling cold, Blood pressure decreased, Blood pressure fluctuation, Dyspnoea, Dizziness, Tachycardia, Drug intolerance, Nausea, Paraesthesia.	Rhinitis allergic, Platelets increased probably reactive, Von Willebrand's, Urticaria (antibiotic)	5 mins after vaccination, numbness and tingling in the arm including hand. Collapsed, blood pressure at 70/50 mmHg. Improvement with passive leg raising and hydration. Metallic taste in mouth, dizziness, red eyes, respiratory problems. Sudden tachycardia and strong shivering/freezing. Improvement with cortisone, blood pressure normal. Doctor diagnosed incompatibility reaction.
		56F	0 day	Resolved	1 day	Rash, Paraesthesia, Vomiting	Not reported	The individual experienced extreme tingling from the ankles up to and including the thighs, like standing in stinging nettles. Skin rash still extreme with severe itching, now treated with cortisone ointment.
		41F	0 days	Resolved	Same day	Urticaria, Rash pruritic, Lip swelling, Dizziness,	Not reported	About 3-4 minutes after vaccine, felt very faint and weird sensation of

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Feeling of body temperature change, Paraesthesia oral, Paraesthesia, Presyncope, Nausea		being dropped into her own body. Lips started to swell and tingling sensation on lips. Generalized itchiness and hives noted on hands, feet, ankles.
4.1(b)		40F	1 day	Resolving	Unknown	Urticaria, Monoplegia, Bradycardia, Vertigo, Stiff tongue, Bone pain, Asthenia, Vertigo, Ecchymosis, Fatigue, Myalgia, Hypoaesthesia, Paraesthesia	Urticaria, Allergy to ibuprofen, capsaicin, dust mite, pecans.	The reporter defines ADR "serious permanent disability". Tests: echo 06-APR-2022, CBC12-MAR-2022, and ECG 06-APR-2022 with no results; LDH 12-MAR-2022 of 235 IU; 225/135. Vaccine start date 0-MAR-2022.
		64F	< 2 months (est)	Unknown	41 days	Dysgeusia, Injection site rash, Headache, Injection site pain, Paraesthesia	Not reported	
		51F	~2 weeks (est)	Unknown	Unknown	Chest pain, Paraesthesia, Rash, Injection site pain, Myalgia, Nausea, Pyrexia	Prinzmetal angina	
		45F	< 4 weeks (est)	Unknown	2 months (est)	Periorbital swelling, Skin discolouration,	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Rhinorrhoea, Pain in extremity, Paraesthesia		
4.1(b) *Med. confirmed	4.1(b)	42F	<1month(est)	Unknown	Unknown	Rash, Circulatory collapse, Cardiovascular disorder, Tinnitus, Heart rate increased, Ear discomfort, Visual impairment, Dizziness, Cold sweat, Headache, Paraesthesia	Not Reported	
4.1(b)	4.1(b)	30F	2 days	Unknown	Unknown	Face oedema, Swelling, Dyspnoea, Diarrhoea, Lymphadenitis, Vision blurred, Anxiety, Injection site pain, Injection site, Myalgia, Paraesthesia	Not reported	Pins and needles in the toes, feet and hands, more dominant on the left side of the body. The feeling would be strong and wake me up at night and I would have trouble falling asleep.

Thirty (30) reports fell within the Hypersensitivity SMQ Narrow. These ICSRs predominantly involved females (n=26) ranging in age between 25 to 65 years. TTO was unknown in 4 reports and ranged from 0 days to less than or equal to 57 days in the remaining reports. Within 12 reports, paresthesia showed a close temporal association to vaccination with a TTO of 0 to 1 days. Two (2) of the 30 individuals had allergic histories.

Four (4) reports of paresthesia occurred in the context of reported anaphylaxis ([redacted] and [redacted]) or potential anaphylaxis [redacted] and [redacted].

Among the remaining reports, facial and perioral swelling, rash, and urticaria were reported. Concomitant medications were reported in only 1 report, which has a potential confounding factor for paraesthesia of Lyrica. Medical history was reported in only 4 reports, 2 of which described allergies.

Based on the data available, the cases in the table above represent paraesthesia in the context of hypersensitivity, and likely not a distinct entity of paraesthesia.

Table 8: Summary Table of Co-Reported Events with Pyrexia

Presented in the table below are the cases with the event of interest co-reported with Pyrexia. The events are sorted by Event Outcome. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information such as concomitant medications and relevant/descriptive details is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		56F	3 days	Not resolved	42 days	Pyrexia, Adnexa uteri pain, Chest pain, Burning sensation, Decreased appetite, Paraesthesia, Influenza like illness, Fatigue, Headache, Arthralgia	Not reported	tingling and numbness in the legs, pins and needles in hands, back aches, random severe pain on calves, in middle of night, oppressive pain in the chest and burning sensation all over the body. Took homeopathic care. Concomitant: Vit D, C
		52F	5 days (est)	Not resolved	76 days	Pyrexia, Arthritis, Somnolence, Fatigue, Paraesthesia	Not reported	
		27F	<1 month (est)	Not resolved	2 months	Pyrexia, Oropharyngeal pain, Chromaturia, Dysgeusia, Dyspnoea, Hot flush, Migraine, Palpitations, Urine odour abnormal, Arthralgia, Malaise, Paraesthesia	Not reported	
		25M	<3 weeks (est)	Not resolved	1 month	Pyrexia, Dizziness, Muscular weakness, Paraesthesia, Arthralgia, Fatigue, Headache, Vomiting	Not reported	Magnesium, lysine

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)	[redacted]	27F	2 months(est)	Not resolved	60 days	Pyrexia, Chest pain, Dyspnoea, Lymphadenopathy, Pruritus, Arthralgia, Fatigue, Headache, Injection site pain, Myalgia, Burning sensation	Not reported	
4.1(b)	[redacted]	31F	70 days(est)	Not resolved	41 days	Pyrexia, Chest pain, Hypoaesthesia, Paraesthesia, Headache, Myalgia, Nausea, Hypoaesthesia, Paraesthesia, Headache, Nausea	Not reported	
4.1(b)	[redacted]	Unk F	1 day	Not resolved	64 days	Pyrexia, Cough, Influenza, Peripheral vascular disorder, Limb discomfort, Paraesthesia, Dizziness, Lymphadenopathy, Fatigue	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		56F	2 day	Not Resolved	75 days	Pyrexia, Oropharyngeal pain, Paraesthesia, Influenza, Breakthrough COVID19, Headache, Nausea	Seasonal allergy(pollen) Drug hypersensitivity(penicillin) Stress	
		62F	Day 0	Not resolved	52 days	Pyrexia, Syncope, Paraesthesia, Cardiovascular disorder, Muscle spasms, Chills, Fatigue, Headache	Mite allergy, Seasonal allergy, Arthritis, Migraine	Pins and needles
		48F	same day	Not resolved	Unknown	Pyrexia, Muscular, weakness, Radiculopathy, Hypoaesthesia, Chills, Headache	Tobacco user	After 2nd dose of vaccination, individual experienced Numbness in face.
		50F	3 days	Not resolved	Unknown	Pyrexia, COVID-19 immunization, Nasopharyngitis, Chest pain, Cardiac discomfort, Oedema peripheral, Arrhythmia, Hypoaesthesia, Pain in extremity,	Not reported	One day after vaccination, she was revaccinated with a different COVID-19 vaccine. 2 days after, numbness of head, pain ankle, heart pressure sensation.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Arthralgia, Burning sensation		
[redacted]		34F	1 day	Not resolved	Unknown	Pyrexia, Hypothermia, Tachycardia, Diarrhoea, Injection site pain, Headache, Paraesthesia,	Not reported	
		Unk M	0 days	Not resolved	4 weeks (est)	Pyrexia, Diarrhoea, Insomnia, Asthenia, Vertigo Tremor, Cough, Nasopharyngitis, Pain in extremity, Myalgia, Paraesthesia	Not reported	Paraesthesia lower limb
		Unk, F	1 day	Not resolved	>4 weeks (est)	Hyperpyrexia, Oropharyngeal pain, Erythema, Vomiting, Headache, Nausea, Injection site reaction, Hypoaesthesia	NA	Facial redness
		51M	1 day	Not resolved		Pyrexia, Chest pain, Hypoaesthesia,	Not reported	Numbness in hand

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Restlessness, Dizziness, Pain in extremity, Fatigue		
[redacted]	[redacted]	46F	Day 0	Resolved with sequelae (unspecified)	4 days	Pyrexia, Arrhythmia, Dyspnoea, Gait disturbance, Ocular discomfort, Dizziness, Fatigue, Headache, Paraesthesia	Pancreatic failure, Autoimmune thyroiditis, HLA-B*27 positive, Aicardi-Goutieres syndrome, Mitral valve disease	Hypotension/sensory disturbance; emotional disorder, upper jaw, neck side and left shoulder
		44F	<10 weeks (est)	Resolving	24 days	Pyrexia, Chest pain, Hyperhidrosis, Paraesthesia, Hyperhidrosis, Paraesthesia	Not reported	
		65F	1 day	Resolving	58 days	Pyrexia, Palpitations, Paraesthesia, Bone pain, Tachycardia, Arthralgia, Pyrexia, Headache, Nausea	Not reported	
		63F	< 3 weeks (est)	Unknown	3 months (est)	Pyrexia Chest discomfort, Dizziness, Paraesthesia, Malaise,	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		26F	66 days(est)	Unknown	51 days	Pyrexia, Chest pain, Dizziness, Paraesthesia, Pain in extremity, Fatigue	Not reported	
		46F	<5 days (est)	Unknown	73 days	Pyrexia, Arrhythmia, Dyspnoea, Hypoaesthesia, Ocular discomfort, Head discomfort, Dizziness, Asthenia, Gait disturbance, Fatigue,	Autoimmune thyroiditis, Pancreatic failure, Mitral valve disease, HLA-B*27 positive, Ill-defined disorder, Hypotension	Numbness upper jaw, side of neck, upper arm Not reported
		43F	1 day	Unknown	Unknown	Pyrexia, Injection site pain, Injection site swelling, Myalgia, Anxiety, Insomnia, Fatigue, Headache, Paraesthesia	Not Reported	shooting pains down arm and into shoulder, was not sleeping and was extremely tired all the time.

Twenty-two (22) reports had co-reported PTs of Pyrexia or Hyperpyrexia. The majority of the ICSRs involved females (n=23), with age ranging from 26 to 63 years. TTO ranged from 0 days to an estimated upper bound of 10 weeks. Within 11 reports, TTO of reports of paresthesia with pyrexia were within 0 to 2 days. Four (4) cases had co-reported events of influenza, one of which also reported breakthrough-COVID infection, and 3 reports had co-reported events of influenza-like-illness. Medical history was reported in 6 cases (3 described allergic histories and 3 autoimmune thyroiditis). Overall, the reports of paresthesia, when reported with fever, appeared to be reflective of systemic reactogenicity as at least half occurring within 3 days of vaccination and with no particular pattern in terms of co-reported symptoms across other body systems.

Table 9: Summary Table of Co-Reported Events with Palpitations, Tachycardia, Heart Rate Increased, Myocarditis, Pericarditis, Carditis

Presented in the table below are the cases with the event of interest, co-reported with a cardiac event of palpitations, tachycardia, or myocarditis. The table below excludes the cases which have already been included in the prior tables. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information such as concomitant medications and relevant/ descriptive details, is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)	[redacted]	34F	1 day	Not resolved	<3 months (est)	Palpitations, Tinnitus, Vomiting, Paraesthesia	Not reported	
4.1(b)	[redacted]	45F	5 days	Not resolved	64 days	Pericarditis, Tachycardia, Chest pain, Dyspnoea, Pneumonia, Confusional state, Dizziness, Lethargy, Pollakiuria, Hypertension, Pain in extremity, Nausea, Electric shock sensation, Burning sensation, Paraesthesia	Not reported	
4.1(b)	[redacted]	46F	(estimate) 3 months	Not resolved	29 days	Pericarditis, Pneumonia, Chest pain, Dyspnoea, Tachycardia, Burning sensation, Confusional state, Dizziness, Echocardiogram abnormal, Electric shock sensation, Paraesthesia, Tremor, Hypertension, Nausea	Not reported	
4.1(b)	[redacted]	30F	Not reported	Not resolved	Unknown	Palpitations, Tachycardia, Hypoaesthesia, Irregular breathing, Paraesthesia,	Not reported	

MER #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		31F	< 4 weeks (est)	Not resolved	2 months (est)	Tachycardia Dyspnoea Paraesthesia	Not reported	
		63F	(estimate) 3 months	Not resolved	36 days	Palpitations, Paraesthesia	Not reported	
		32 F	21 days	Not resolved	78 days	Tachycardia Blood pressure increased Hypoaesthesia, Pain in extremity, Paraesthesia	Seasonal allergy Lipoedema Ill-defined disorder Fibromyalgia	Relevant lab tests included: Blood pressure measurement (Result: Increased blood pressure 183/100; 20-MAR-2022) Medical history included Lipoedema, CVI, Fibromyalgia. Hospitalization in cardiological and neurological department.
		46F	2 days	Not resolved	N/A	Tachycardia, Palpitations, Paraesthesia, Dizziness, Nausea, Paraesthesia	Not Reported	1 day after vaccination, she experienced tachycardia ,2 days after vaccination-tingling, heart racing, tingling of extremity, paresthesia, nausea, dizziness.
		53F	<3 weeks (est)	Not resolved	42 days	Palpitations, Dyspnoea, Concomitant disease aggravated, Decreased	Not reported	Vitamin D3

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						appetite, Diarrhoea, Feeling abnormal, Paraesthesia, Chills, Headache, Injection site pain, Malaise, Nausea		
[redacted]	[redacted]	44F	Primary	Not resolved	2 months	Palpitations, Atrial flutter, Chest discomfort, Eye pain, Joint stiffness, Lacrimation increased, Muscular weakness, Headache, Paraesthesia	Not reported	
		43F	Unknown	Not resolved	Unknown	Palpitations, Chest discomfort, Chest pain, Confusional state, Frequent bowel movements, Head discomfort, Neuralgia, Pollakiuria Pruritus, Fatigue, Headache, Nausea, Burning sensation, Paraesthesia	Not reported	
		56F	0 days	Not resolved	3 days	Tachycardia, Dry throat, Cough, Nasal congestion, Dizziness, Nasopharyngitis,	Asthma, Mechanical urticaria Photosensitivity reaction, Food and	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Asthma, Malaise, Paraesthesia	Seasonal allergy	
4.1(b)	[redacted]	Unk M	2 days	Not resolved	Unk	Tachycardia, Photopsia, Limb discomfort, Visual field defect, Myalgia, Headache, Paraesthesia	Drug hypersensitivity Iodine allergy Influenza like illness Pyrexia Cough Nasopharyngitis Chills Palpitations Hypoaesthesia Headache Arthralgia	Medical history: Allodynia, Arthralgia, Chills, Cough, Drug hypersensitivity, Headache, Hypoaesthesia, Influenza like illness, Iodine allergy, Nasopharyngitis, Palpitations, Pyrexia and Visual field defect. concomitant medications: Cortisone and Bisoprolol. Initially flu-like symptoms with fever cough cold chills palpitations and numbness in the right side of the body and especially in the face. Associated with headache and joint pain. After a short period of improvement, these symptoms recur again and again. Treated with cortisone and bisoprolol for the tachycardia. Cortisone does not help. At the same time, there was a restriction of the field of vision on the right. A consultation with an ophthalmologist was

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								obtained. Only a test of the visual field restriction showed a result. Brain MRI, no findings. According to the doctors, everything was inconspicuous here. In the meantime, the numbness feelings have partially changed into painful stimuli. A consultation with a neurologist is scheduled.
4.1(b)	[redacted]	33M	11 days	Not resolved	8 weeks (est)	Palpitations, Feeling abnormal Apathy, Sleep disorder, Tremor, Disturbance in attention, Dizziness, Fatigue, Paraesthesia	Allergy to amoxicillin	11 days after Nuvaxovid, pain in the leg, followed by severe dizziness and drowsiness, which ended in hospitalization. A short time later, the second hospital stay should follow, reasons: severe drowsiness, tachycardia, shaky hands. However, without significant findings on the part of the hospital. I have had a doctor's marathon, ENT, orthopedist, family doctor etc. but no one can help me so far.
4.1(b)	[redacted]	43F	<3weeks (est)	Not resolved	2 months	Palpitations, Chest discomfort, Chest pain,	Not reported	Neuralgia - Creeping, burning inside neck and along spine. Stabbing,

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Neuralgia, Confusional state, Frequent bowel movements, Head discomfort, Pollakiuria, Pruritus, Fatigue, Headache, Nausea, Burning sensation		burning nerve endings across entire body including eyeballs and inside ears.
4.1(b)	[redacted]	Unk F	Unknown	Not resolved	unknown	Palpitations, Hypoaesthesia, Muscle spasms, Restlessness, sleep disorder, Thirst, Pain in extremity, Arthralgia, Headache, Vomiting, Paraesthesia	Not reported	
4.1(b)	[redacted]	27M	Unknown	Not resolved	2 months (est)	Dyspnoea Heart rate increased, Hypoaesthesia Muscle spasms, Productive cough, SARS-CoV-2 test positive, Wheezing, Fatigue, Injection site pain	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b) * Med conf	4.1(b)	53F	0 days	Resolved	0 days	Tachycardia Abdominal pain upper Paraesthesia	Contrast media and drug allergy	paresthesia in the site peribuccal and prelipithimic episode
4.1(b)	[redacted]	52F	1 day	Resolved	10 days	Tachycardia, Dizziness, Visual impairment, Trigeminal neuralgia, Renal pain, Headache, Fatigue Myalgia, Hyperaesthesia	Not Reported	1 day after vaccination, she experienced tachycardia and head pain , 2 days after vaccination- myalgia, vision decreased, trigeminal neuralgia on the left side more than on the right with hyperesthesia of the facial skin, generalized tooth pain, tingling of the scalp and fatigue, 3 days after vaccination- dizziness, kidney pain, interval training on both sides combined with severe pain and local freezing cold in the area of the kidneys and hyperesthesia on the left forearm, as well as pulling in the chest area. Within 6 weeks, all symptoms have largely subsided.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)	4.1(b)	25M	< 1 Week (est)	Resolving	< 5 weeks	Palpitations, Tinnitus, Presyncope Paraesthesia	Not reported	
4.1(b)	4.1(b)	50F	0 days	Resolving	6 weeks (est)	[Palpitations*not coded], Chest discomfort, Hypoaesthesia, Dizziness, Dyspnoea Fatigue, Headache Injection site pain	Not reported	After vaccine I felt numbness on the right side of face. Then numbness on left arm and then numbness at back of left knee and leg. Fatigue, dizziness and headache on the day of vaccine. Second day only injection site pain. Seventh day I had a strong stabbing chest pain with shortness of breath, lasting for about 2 or 3 hours. Ninth day I had a leg pain in the middle of the night that lasted for one day. The pain went away and came back three days later more persistent for about three days. After chest pain I had many episodes of chest tightness with shortness of breath and **palpitations**.
4.1(b)		43F	<7 weeks (est)	Resolving	54 days	Carditis, Pyrexia, Cardiac disorder, Chest pain, Heart rate irregular, Exercise	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						tolerance decreased, Influenza like illness, Headache, Fatigue, Injection site pain, Nausea, Hyperaesthesia		
4.1(b)		31F	4 days	Resolving	69 days	Arrhythmia, Dyspnoea, Chest pain, Tenderness, Fatigue, Headache, Paraesthesia, Hypoaesthesia,	Autoimmune thyroiditis, Hypothyroidism	Numbness in face, Tingling
		42F	2 days	Unknown	Unknown	Heart rate increased, Chest pain, Facial paralysis, Disorientation, Concomitant disease Aggravated, Diarrhoea, Dizziness, Dyspnoea, Paraesthesia, Fatigue, Headache	Arrhythmia, Gastroesophageal reflux disease, Depression, Anxiety, Non-tobacco user, Abstains from alcohol	Novavax administered by 3:30 pm and by evening felt disoriented and extremely tired. 2 days later, had increased heart rate, radiating chest pain into the neck and down the left arm, with tingling and numbness in the same arm. ED visit with blood tests, ECG, CXR and cardio referral. 2 weeks later still fatigued and SOB.
		62F	< 1 Week (est)	Unknown	2 months (est)	Pericarditis, Palpitations, Arrhythmia, Ataxia, Axillary lymphadenectomy,	Brugada syndrome, Pericarditis, Hyperinsulinaemia, Hypersensitivity,	March 2nd 2022 1st Novavax vaccination. No reaction at the time or for the following 36 hrs. 36 hrs later “Normal” (to be

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Back pain, Chest pain, Chills, Decreased appetite, Disturbance in attention, Dizziness, Dysphagia, Dyspnoea, Eructation, Hyperhidrosis, Hypoglycaemia, Inflammation, Injection site discomfort, Lethargy, Migraine, Muscle spasms, Myalgia, Pain, Respiration abnormal, Tremor, Paraesthesia	Spinal fracture, Hypoglycaemia, Pleurisy	expected) muscle aches, lethargy and discomfort around injection site. Sat March 5th those symptoms had dissipated but during the afternoon I got pain in left chest & belching started. Unable to lay flat on my back. Pain less when sitting.4th day after Novavax Trouble swallowing, choking at times when trying to eat, this continued for about 10 days. Left chest felt swollen heavy and discomfort around heart area. Intermittent sweats Short of breath Very dizzy Tight upper back and neck. Thumping Arrhythmia's intermittently in L chest Extreme lethargy Belching. Pain less when sitting. Couldn’t tolerate bra pressure – for next 2 weeks Hypoglycemic episodes. (Haven’t experienced hypoglycaemia for 9 months). Muscle cramps not

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								just aches. 5th day after Novavax Pain increased in T6 area in back (where I had a fracture last year) and through the upper spine/neck felt very inflamed. Intermittent piercing pain in left chest continued until day 10. Dizzy Belching Lymph gland slightly tender in left armpit. (Only for 1 day). 8th day after immunization, pain when lifting arms above chest height – e.g. at clothesline or to wash hair. Diagnosed with Pericarditis by Cardiologist and began Colchicine. Pericarditis for the 3rd time in 9 months. 10th & 11th day after Novavax: Pain subsiding. Pain in T6 and upper back after lifting arms. 13th day after Novavax, woke 4am with torso feeling inflamed internally and upper back. Couldn't tolerate bra pressure. Reaching above chest induced back pain and

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								slight breathing discomfort. Bed rest 4 x during day.15th day after Novavax, felt great. Did not need the usual 2 or 3 sleeps during the day. However, muscle pain in left neck and left upper back continued intermittingly for days following and still needed to rest and overcome shortness of breath any time after attempting any physical task. 3 weeks after Novavax: all chest symptoms dizziness & extreme lethargy non-existent. Intense muscle aches non-existent but have ongoing muscle stiffness and pain and a feeling of some inflammation in upper back-neck-shoulders. Requiring massage several times a day. Still unable to lay on left side without pain in left ribs/chest and heavy feeling in chest when sleeping. Alleviated by not laying on side. Still can't

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								tolerate bra pressure after an hour or so. Belching continues. Advised by Cardiologist to continue Colchicine for 3 months and not to have 2nd Novavax on 23rd March having had Pericarditis 3 times and Pleurisy once in the last 9 months.
4.1(b)	4.1(b)	51F	2 days	Unknown	Unknown	Pericarditis, Palpitations, Angina pectoris, Chest pain, Chest discomfort, Dizziness, Hypoaesthesia, Insomnia, Neck pain, Pain, Paraesthesia	Neurological symptom, Dizziness	Concomitant Colchicine
4.1(b)		59 F	Unknown	Unknown	Unknown	Palpitations, Headache, Paraesthesia	Not reported	
4.1(b)		36F	6 days 18 hrs. 15 min	Unknown	Unknown	Palpitations, Chest discomfort, Dizziness, Dyspnoea, Abdominal pain, Vision blurred, Fatigue, Headache, Myalgia, Nausea, Injection site pain,	Not reported	6 days 18 hrs. 15 mins after vaccination, a 36-year-old started to experience all mentioned PTs including pain in chest and shoulder that radiated down left arms and right fingers, irregular

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Injection site swelling, Paraesthesia		heart rate and low blood pressure.
4.1(b) [redacted]	[redacted]	59 M	same day	Unknown	Unknown	Myocarditis, Dizziness, Atrial fibrillation, Paraesthesia, Left ventricular failure	Not Reported	On same day of vaccination, he experienced tingling feet/hands, Atrial fibrillation, Paresthesia, Dizziness, Left ventricular failure and Myocarditis, All the events were considered as serious ,hospitalization and medically significant.

Twenty-nine (29) cases were classified in the table above. One case (4.1(b)) described palpitations; however, this PT was not a coded term. Four (4) of the cases occurred in the context of pericarditis, 1 each in the context of myocarditis, carditis, and unspecified arrhythmia. For the remaining 22 cases, no clear diagnosis was provided. These cases involved 5 males and the remaining were females, with an age range of 25 to 65, when reported. None contained significant medical history or concomitant medication information. Four (4) paraesthesias and dysaesthesias HLT events were reported as resolved or resolving in less than 5 weeks. The outcome for the remaining was either unknown or not resolved. The constellation of co-reported PTs in these cases did not reveal a syndrome or a pattern.

Table 10: Summary Table of Co-Reported Events with Chest Pain or Chest/Cardiac Discomfort

Presented in the table below are the cases with the event of interest, co-reported with chest pain or chest/ cardiac discomfort. The table below excludes the cases which have already been included in the prior tables. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information, such as concomitant medications and relevant/ descriptive details, is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		49F	0 days	Not recovered	57 days	Chest pain, Paraesthesia oral, Hypoaesthesia oral Burning sensation, Dyspnoea, Back pain, Speech disorder, Tremor, Pain in extremity, Headache, Paraesthesia,	Not reported	Tingling around [mouth and] nose; tingling 4th toe left foot, Burning left palm
		33F	Same day	Not resolved	88 days	Chest pain, Dyspnoea, Dysgeusia, Vision blurred, Dizziness, Paraesthesia	Food allergy, Migraine with aura, Familial risk factor, Iron deficiency anaemia	
		48F	1 day	Not resolved	2 months	Chest pain, Dyspnoea, Lethargy, Skin burning sensation, Tinnitus, Headache, Paraesthesia,	Not reported	tingling down the face, and feels pressure in chest, slight pain in the heart, steady burning sensations in the arm, loud ringing in the ears.
		35M	Not reported	Not resolved	Not reported	Chest pain, Ear infection, Paraesthesia, Headache	Not reported	Paraesthesia (Pins and needles in head)
		58F	< 4 weeks (est)	Not resolved	2 months (est)	Chest pain, Dizziness, Muscular weakness, Fatigue, Headache, Myalgia, Paraesthesia	Not recovered	
		36M	< 4 weeks (est)	Not resolved	2 months (est)	Chest pain, Chest discomfort, Hypertension, Dyspnoea, Sleep paralysis, Paraesthesia	Not reported	
		41M	< 4 weeks (est)	Not resolved	2 months (est)	Chest discomfort, Chest pain, Hypertension, Dyspnoea, Disorientation, Irritability, Migraine, Sleep terror, Fatigue, Paraesthesia	Not reported	
		51F	2 months (est)	Not Resolved	1 month	Chest pain, Back pain, Lacrimation increased, Swelling, Lymphadenopathy, Pain in extremity, Pruritus, Burning sensation	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		31F	2 months (est)	Not resolved	26 days	Chest pain, Dyspnoea, Abdominal pain, Diarrhoea, Paraesthesia	Not reported	
		54M	54 days (est)	Not resolved	50 days	Chest pain, Visual impairment, Pain in extremity, Headache, Paraesthesia	Not reported	
		49F	33 days (est)	Not resolved	57 days	Chest pain, Poor peripheral circulation, Back pain, Dyspnoea, Hypoaesthesia, Paraesthesia oral, Pain in extremity, Headache	Not reported	
		30F	70 days (est)	Not resolved	47 days	Chest pain, Paraesthesia	Not reported	
		29F	Unknown	Not Resolved	2 months (est)	Chest pain, Paraesthesia, Fatigue	Not reported	
		37F	Unknown	Not Resolved	2 months (est)	Chest pain, Paraesthesia, Arthralgia	Not reported	
		40M	Unknown	Not Resolved	Unknown	Chest pain, Dyspnoea, Paraesthesia, Headache, Arthralgia, Injection site pain, Myalgia	Not reported	
		57F	Unknown	Not Resolved	2 months (est)	Chest discomfort, Dyspnoea, Hypoaesthesia	Not reported	
		68F	Unknown	Not Resolved	2 months (est)	Chest discomfort Chest pain, Hypertension, Headache, Paraesthesia	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		51F	Unknown	Not Resolved	Unknown	Chest discomfort, Chest pain, Dizziness, Hypoaesthesia	Not reported	Secondary suspect medication was reported: Spikevax COVID-19 vaccine (Elasomeran (mRNA) on an unspecified date
		55F	5 days	Not resolved	N/A	Non-cardiac chest pain, Renal pain, Muscle twitching, Dysaesthesia	Photo-sensitivity reaction, Sun allergy	
		46M	1 day	Not resolved	85 days	Chest discomfort, Hypertension, Pain in extremity, Headache, Paraesthesia	Coronavirus infection, Atypical pneumonia	
		30F	Unknown	Not resolved	<1 month est.	Musculoskeletal chest pain, Pain, Headache, Paraesthesia	Wolff-Parkinson-White syndrome	Tingling of extremity, left
		57F	Day 0	Not resolved	72 days	Cardiac discomfort, Tension headache, Paraesthesia	Not reported	Paresthesia in the whole body
		50M	<3 days (est)	Ongoing	36 days	Chest pain, Chest discomfort, Paraesthesia, Pleurisy, Abdominal pain, Headache	Not reported	Paraesthesia - Pins and needles sensation through arms, has been up and down left side.
		48F	<3weeks (est)	Recovering	74 days	Chest pain, Chest discomfort, Dyspnoea, Head discomfort, Musculoskeletal chest pain, Paraesthesia, Tinnitus, Hypoaesthesia, Pain in extremity, Fatigue, Nausea, Burning sensation	Not reported	Face tingling, head pressure, and burning sensation of arms.
		53F	2 days	Recovering	NA	Chest pain, Dizziness, Hemiparaesthesia, Hypoaesthesia, Paraesthesia	Not reported	Numbness of the right half face and of the right arm

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		48F	<3weeks (est)	Recovering	Unknown	Chest pain, Dyspnoea, Burning sensation, Chest discomfort, Head discomfort Musculoskeletal chest pain Paraesthesia, Tinnitus, Hypoaesthesia, Pain in extremity, Fatigue, Nausea	Not reported	A 48-year-old female, with reported past history of Iron deficiency, Congenital cystic kidney disease, Endometriosis, Ovarian cyst, Microalbuminuria who experienced Burning sensation, Chest discomfort, Chest pain, Dyspnoea, Fatigue, Head discomfort, Hypoaesthesia, Musculoskeletal chest pain, Nausea, Pain in extremity, Paraesthesia and Tinnitus. Face tingling, head pressure, and burning sensation of arms.
		43F	Day 0	Recovering	78 days	Cardiac discomfort, Muscular weakness, Headache, Fatigue, Nausea, Paraesthesia	Not reported	43-year-old F experienced Paraesthesia on day 0 of primary dose with Nuvaxovid. The event was recovering.
		35F	<3 weeks (est)	Resolved	Unknown	Chest discomfort, Abdominal pain upper, Nausea, Hypoaesthesia, Paraesthesia	Not reported	
		28F	<2 weeks (est)	Resolved	79 days	Chest pain, Confusional state, Cyanosis, Lethargy, Neck pain, Paraesthesia, Tinnitus, Pain in extremity, Fatigue, Headache, Nausea	Not reported	
		41F	Unknown	Resolving	Unknown	Chest pain, Paraesthesia Pain in extremity	Not reported	
		32F	Same day	Resolving	14 days	Chest discomfort, Dyspnoea, Paraesthesia, Fatigue	Not reported	Chest discomfort that started as sporadic, very mild within an hour of the injection and became more intense over the following days, particularly after 48 hours and it was usually accompanied with shortness of breath and overall fatigue. She experienced shooting pains under her right arm, mild neck pain and occasional tingling feeling in her fingers.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		43F	7 days	Unknown	N/A	Chest pain, Back pain, Influenza, Weight increased, Hypoaesthesia	Not reported	7 days after vaccination, back pain in the chest area, chest pain, flu symptoms and numbness in the left arm. Also, weight gain of 3- 4 kilos. It feels like an allergic reaction to vaccination. I have had a runny nose, watery eyes for 6 weeks. This pain in the chest area, also on the back comes again and again. I went to my doctor, and she said that it wasn't because of the vaccination.
		50F	Same day	Unknown	13 days	Chest discomfort, Fatigue, Anxiety, Headache, Paraesthesia	Not reported	also experienced itching without rash

Thirty-two (32) reports of paresthesia-related events with co-reported chest pain/discomfort that were not previously reviewed among the reports of no or minimal co-reported events, hypersensitivity reactions, pyrexia, or cardiac were reviewed. The majority of the ICSRs involved females (n=25) ranging in age from 27 to 68 years. The 7 males ranged in age from 31 years to 54 years. Reported TTOs (n=25) ranged from 0 days to an estimated upper bound of 3 weeks. There was no temporal clustering of reports. A subset of cases co-reported PTs of hypertension (n=4). Overall, no trends are noted among the reports of paresthesia when co-reported with chest pain and/or discomfort.

Table 11: Summary Table of Co-Reported Events with Dizziness

Presented in the table below are the cases with the event of interest, co-reported with Dizziness. The table below excludes the cases which have already been included in the prior tables. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information such as concomitant medications and relevant/ descriptive details, is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		59 F				Dizziness, vision blurred, Discomfort, Aggression, Abdominal pain, Rheumatic disorder, Bone pain Condition aggravated, Pain in extremity, Chills, Nausea, Myalgia, Paraesthesia,	Allergy to metals Allergy to chemicals Rheumatic disorder Chronic obstructive pulmonary disease	
		Unk F	3 days	Not resolved	69 days	Dizziness, feeling abnormal, Blood pressure increased, Dysgeusia, Fatigue, Nausea Hypoaesthesia		
		42 F	<2 weeks (est)	Not resolved	44 days	Dizziness Head discomfort, Axillary pain, Decreased appetite, Diarrhoea, Hypoaesthesia, Limb discomfort, Musculoskeletal stiffness, Pain, Paraesthesia, Chills, Pain in extremity, Pruritus, Fatigue, Headache		
		38 F	<1 week (est)	Not resolved	1 month	Dizziness Arthritis, Conjunctivitis, Oropharyngeal discomfort, Paraesthesia	Not reported	
		36 M	Unknown	Not resolved	2 months (est)	Dizziness, Head discomfort Concomitant disease aggravated Muscle spasms Muscle twitching Arthralgia Fatigue Headache Injection site pain Paraesthesia	Not reported	Concomitant medication: Symbicort
		F	Same day	Not resolved	70 days, ongoing	Dizziness, Paraesthesia, Fatigue, Nausea	Not reported	
		F	Same day	Not resolved	73 days, ongoing	Dizziness, Hypoaesthesia, Ear discomfort Paraesthesia	Not reported	
		43 F	2 days	Not resolved	71 days, ongoing	Dizziness, Loss of consciousness Vision blurred, , Somnolence, Diarrhoea, Vertigo positional, Disturbance in attention, Gait disturbance, feeling abnormal, Diplopia, Hypotension, Fall, Asthenia, Peripheral coldness, Feeling drunk, Confusional state, Hypotonia, Malaise, Fatigue,	Vertigo positional, Dermatitis contact, Seasonal allergy, Mitral valve prolapse, Blood cholesterol abnormal	Concomitant medication: Thomapyrin classic

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Nausea, Myalgia, Headache, Paraesthesia		
4.1(b)		43 F	1 day	Not resolved	62 days, ongoing	Dizziness, Feeling abnormal, Diarrhoea, Paraesthesia, Disturbance in attention, Fatigue	Not reported	
		49 F	7 days	Not Resolved	unknown	Dizziness, Feeling abnormal. Cough Dysgeusia, Disturbance in attention Tension Oropharyngeal pain Dyspepsia Flank pain Feeling cold Hypotonia Hot flush Blood pressure abnormal Sensation of foreign body Headache, Fatigue, Nausea, Paraesthesia	Allergy to plants Allergy to chemicals Allergy to animal	On same day of vaccination she experienced discomfort, cough, one day after vaccination -metallic taste in mouth, impaired concentration in the evening,2 days after -heart burn, dizziness, slightly shivering, tiredness, stabbing pain in the left flank,3 days after vaccination-floppiness,4 days after vaccination-hot face,5 days after vaccination- blood pressure abnormal and foreign body sensation in the throat; constricted , 7 days after vaccination-tingling legs-feet; changing less to strong history tingling nausea and extremely cold blue aching hands and feet ,discomfort of right facial half, pulling in right eyebrow, warmth, heavy half of the face. Relevant lab tests included: SARS-CoV-2 test (Result: Negative ; unspecified date). waiting for second appointment with the neurologist.
		55 F	Same day	Not resolved	2 days	Dizziness, Cough, Hypoaesthesia, Dry mouth, oral Rhinorrhoea, Feeling hot, Dry throat, Pain in extremity, Headache, Paraesthesia	Photosensitivity reaction Sunscreen sensitivity	
		41 F	<2 weeks (est)	Resolved	1 month	Dizziness, Burning sensation,	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		49 F	< 2 weeks (est)	Resolving	3 months (est)	Dizziness, Discomfort, Dyspnoea, Epistaxis, Hypoesthesia, Migraine, Muscle spasms, Muscular weakness, Hypertension, Fatigue Paraesthesia,	Not reported	
		55 F	< 4 weeks (est)	Resolving	2 months (est)	Dizziness, Suicidal ideation, Back pain, Depressed mood, Lethargy, Panic attack Paraesthesia Pain in extremity, Arthralgia Myalgia	Not reported	
		61 F	Unknown	Resolving		Dizziness Loss of consciousness Paraesthesia	Not reported	
		35 F	0 days	Resolving	unknown	Dizziness, Presyncope, Anxiety, Pallor, Injection site pain, Paraesthesia,	Not reported	
		30 F	<1 week (est)	Unknown	49 days	Dizziness, Vertigo, Peripheral swelling, Headache, Injection site pain, Nausea Paraesthesia		
		Unk, M	3 months (est)	Unknown	Unknown	Dizziness, Presyncope, Mental impairment, Abdominal pain upper, Altered visual depth perception, Asthenia, Chromaturia, Concomitant disease aggravated, Confusional state, Coordination abnormal, Cough, Diarrhoea, Disorientation, Dysgeusia, Dyspnoea, Exercise tolerance decreased, Feeling abnormal, Feeling cold, Gait disturbance, Hot flush, Hyperacusis, Hyperhidrosis, Hypoaesthesia, Hypopnoea, Lethargy, Memory impairment, Muscle tightness, Muscular weakness, Nasal congestion, Oropharyngeal pain, Pain, Paraesthesia, Photophobia,	White matter lesion, Retinal disorder	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Skin odour abnormal, Speech disorder, Swelling, Tremor, Vision blurred, Visual impairment, Vitreous floaters, Chills, Headache		

Eighteen (18) cases were classified in the table above. These cases involved 2 males (36 years old, unknown) and the remaining were females, when reported. None contained significant medical history or concomitant medication information. Nine (9) cases had co-reported PTs suggestive of the event of interest occurring in the context of a syncopal or pre-syncopal episodes. There were: loss of consciousness (n=2), presyncope (n=2), feeling abnormal (n=3), and head discomfort (n=2). There remaining ICSRs are not suggestive of any specific context or etiology.

Table 12: Summary Table of Co-Reported Events with Muscle Spasms, Muscle Twitching, or Muscle Involuntary contractions

Presented in the table below are the cases with the event of interest, co-reported with Muscle spasms, Muscle twitching, or Muscle involuntary contractions. The events are sorted by Event Outcome. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information such as concomitant medications and relevant/ descriptive details, is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		33F	0 days	Not resolved	Unknown	Muscle twitching Paraesthesia, Hot flush Vision blurred Peripheral swelling Pain Menstrual disorder Tissue irritation Musculoskeletal stiffness Ear pain Muscle tightness, Lymphadenopathy Pain in extremity Headache	Not reported	The whole right-hand side of the body is affected. Additionally, they felt a chemical irritation (PT: Tissue irritation) and everything on that side (right) is stiff. There is good mobility on left but right side is stiff and swollen and tight. Concomitant medication: aspirin
		Unk, F	0 day	Not resolved	Unknown	Muscle contractions involuntary Burning sensation, Abdominal discomfort, Dyspnoea Heart rate decreased Pain in extremity Fatigue Vaccination site reaction	Not reported	Concomitant medication: cetirizine
		55F	5 days	Not resolved	Unknown	Muscle twitching, Non-cardiac chest pain, Renal pain, Dysaesthesia	Photo-sensitivity reaction, Sun allergy	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		30F	<2 weeks (est)	Not resolved	55 days	Muscle twitching, Paraesthesia, Lymphadenopathy, Headache		
		Unk, F	<1 week (est)	Not resolved	55 days	Muscle twitching, Essential tremor, Paraesthesia		
		58F	Same day	Resolved	One day	Muscle spasms, Paraesthesia, Herpes zoster, Condition aggravated, Seasonal allergy, Neuralgia, Injection site pain	1. Seasonal allergy 2. Penicillin allergy 3. Herpes zoster 4.Hay fever	On the same day after vaccinations, she experienced muscle spasms, numbness of legs .On the same day, after her second vaccination she experienced injection site pain ,13 days after vaccination- Facial Rose- Herpes Zoster ,one month later condition worsened ,pollen allergy with unusual intensity and massive productive cough and runny nose, nerve pain in the upper arm intensity increasing. The event outcomes of Injection site pain and Neuralgia were Not Recovered, Condition aggravated, and Seasonal allergy was Recovering, Herpes zoster was Recovered. Herpes Zoster: immediate treatment with Zostex and vitamin B complex. Hay fever: cetirizine and sinupret.
		59M	Unknown	Resolved	2 months (est)	Muscle spasms, Paraesthesia, Arthralgia, Injection site reaction	Not reported	
		41F	6 days	Resolved	17 days	Muscle twitching Paraesthesia Peripheral swelling Pruritus Erythema	1. Polyneuropathy 2.Rhabdomyosarcoma 3. Breast cancer	6 days after vaccination with dose 1, she experienced uncontrolled twitching of the left toe , several times a minute and tingling/burning in the feet usually noticeable before going to bed, a day after vaccination with dose 2, she experienced oval rash, , swollen , itchy , red and warm. Relevant lab tests included: nerve conduction velocity (Result: mild consequences of chemotherapy-related polyneuropathy; unspecified date) and magnetic resonance imaging head (Result:

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								inconspicuous; unspecified date). Mild consequences of chemotherapy-related polyneuropathy are currently visible in the measurement of nerve conduction velocity. The twitching of the toe has been clarified neurologically. Started after the first vaccination. In the first two weeks several times a minute. Later it became increasingly rare. Has not been treated. After the second vaccination, the twitching of the toe was still present. This was not at the injection site, but at the front of the upper arm. The spot was swollen, red, warm and very itchy. The swelling went back after 3 days. The redness, warmth and itching remained. Cooling has relieved symptoms
4.1(b)		57M	18 days	Resolving	55 days	Muscle twitching, Myalgia, Vaccination site joint pain, Paraesthesia, Injection site pain,	Not reported	
		38 F	2 days	Resolving	Unknown	Muscle twitching Asthenia Limb discomfort Dysaesthesia	Mite, house dust, and pollen allergy	The regulatory authority sender comment is as follows: Are you or the affected person aware of allergies? If so, which ones? Yes, house dust and pollen allergy Information on risk factors or pre-existing conditions not known / no treatment so far, clarification by MRI planned Course: Complaints have improved / are declining
		29F	Unknown	Not resolved	Unknown	Musculoskeletal stiffness Inflammation, , Paraesthesia, Influenza like illness, Injection site reaction	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b) [redacted]	[redacted]	54F	<1 month(est)	Not resolved	Unknown	Muscle spasms Taste disorder Paraesthesia Headache	Rheumatoid arthritis	One day after vaccination she experienced muscle cramps, taste abnormality, headache .and on unspecified date after vaccination-paresthesia . Concomitant medications reported were unspecified immunosuppressives and cortisone .No additional information is expected 1. CORTISONE.

Twelve (12) cases were classified in the table above. These cases involved 2 males (57 and 59 years old) and the remaining were females, when reported. None contained significant medical history or concomitant medication information. In one (1) report, 4.1(b) [redacted], paraesthesia is possibly due to chemotherapy. The remaining ICSRs are not suggestive of any specific context or etiology.

Table 13: Summary Table of Co-Reported Events with Myalgia

Presented in the table below are the cases with the event of interest, co-reported with Myalgia. The table below excludes the cases which have already been included in the prior tables. The Time to Onset (TTO) is estimated, where possible, providing the outer-bound estimation, delineated with a notation of "(est)". If not reported, the duration of the events is estimated from the available start date of the event and the follow-up date, when possible. Additional information such as concomitant medications and relevant/ descriptive details, is provided in the Additional Information column, when available.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		30F				Myalgia, Paraesthesia, Injection site erythema, Injection site pain, Injection site swelling	Not reported	
		56F	<2 weeks (est)	Not resolved	1 month,	Myalgia Anxiety, Blepharospasm, Bone pain, Confusional state, Eye discharge, Insomnia, Neck pain, Paraesthesia, Pollakiuria, Pain in extremity, Headache,	Not reported	
		36M	Unknown	Not Resolved		Myalgia Abdominal pain Hypoaesthesia Lethargy Neuralgia Paraesthesia Arthralgia Nausea Vomiting	Not reported	
		60M	< 1 week (est)	Not Resolved		Myalgia Cough Limb discomfort Hypoaesthesia Tonsillar hypertrophy Local reaction Hypoaesthesia Influenza like illness Injection site pain Arthralgia Fatigue	Blood pressure increased Unspecified Treatment and Symptomatic treatment	
		35F	5 days	Not resolved	75 days	Myalgia Sensory level abnormal Hypoaesthesia Paraesthesia Groin pain Lymphadenopathy Pain in extremity. Injection site pain Fatigue	Food allergy Migraine with aura Familial risk factor Iron deficiency anaemia	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		36 M	1 day	Not resolved	46 days	Myalgia, Paralysis, Enthesopathy, Neuralgia, Joint stiffness, Enthesopathy, Hypoaesthesia, Dysaesthesia, Hypoaesthesia, Autoantibody positive, Dehydroepiandrosterone decreased, Hypovitaminosis, C-reactive protein increased, Calcium ionised, decreased Blood creatine, phosphokinase increased, Fatigue	Hypertension Osteoarthritis	
		41F	Same day	Not resolved	70 days	Myalgia, Polyneuropathy, Influenza, Paraesthesia, Hypomenorrhoea, Paresis, Disturbance in attention, Memory impairment, Chills, Injection site pain, Headache, Fatigue, Arthralgia, Vomiting, Nausea	Myopia	
		41F	Same day	Not resolved	Unknown	Myalgia Paraesthesia Myalgia	Seasonal allergy, Perfume sensitivity, Allergy to metals	The following medical history was reported: Allergy to metals, Perfume sensitivity, Seasonal allergy and Hypersensitivity to Cotrim (trimethoprim/sulfamethoxazole). Treatment included: treatment at hospital with prednisolone, electrolytes and aspirin. The regulatory authority's senders' comment is as follows: Are you or the

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								affected person aware of any allergies? If yes, which ones? Hay fever, fragrances, Cotrim, nickel / 08.04.2022 only vaccine arm affected by symptoms, then spread to other arm and right leg, numbness of throat and nose, treatment in hospital with prednisolone, electrolytes, aspirin
4.1(b) *Medically confirmed	4.1(b)	52M	1 day	Recovering	75 days	Myalgia, Paraesthesia, Peripheral swelling	Hypertension	
4.1(b)		42M	within a month (estimate)	Resolved	within a month (estimate)	Myalgia Muscular weakness Burning sensation Hypertension Pain in extremity Arthralgia Vaccination site pain Fatigue	COVID-19 Polymers allergy	
4.1(b)		41M	30 minutes	Resolving	1 day	Myalgia Diarrhoea, Eustachian tube disorder, Hyperhidrosis, Hypoaesthesia, Migraine, Fatigue,	Not reported	
4.1(b)		57F	0 days	Unknown		Myalgia, Paraesthesia Malaise Fatigue	NA	

Twelve (12) cases were classified in the table above. These cases involved 6 males, age range 36-60 years, and 6 females with age range 35-57 years. None contained significant medical history or concomitant medication information. The ICSRs are not suggestive of any specific context or etiology.

Table 14: Summary Table of Co-Reported Events with Muscle Symptoms

Presented in the table below are the cases with the event of interest, co-reported with muscle symptoms.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		30F	<2 weeks (est)	Not resolved	77 days	Muscular weakness Paralysis, Hypoaesthesia, Paraesthesia, Peripheral swelling, Vertigo, Nervous system disorder,	Not reported	
		43F	Unknown	Not resolved	2 months (est)	Muscular weakness Cough Hypoaesthesia Migraine Oropharyngeal pain Paraesthesia Rhinorrhoea Injection site pain	Not reported	
		51F	1 day	Resolved with sequelae (unspecified)	Unknown	Muscular weakness Hypoaesthesia Injection site pain Fatigue Injection site swelling	Allergy to resorcinol, thiomersal, potassium dichromate, propylene glycol Allergy to plants (mugwort, dandelion, nettle) Lactose intolerance, Gluten sensitivity, Seasonal allergy (pollen, grass) Allergy to metals (gold mine) Food allergy (plantain)	On the day of vaccination, she experienced tiredness and exhaustion, upper arm pain and swollen, injection site swelling. One day after vaccination -weakness of limbs, powerlessness in the arm and leg, falling asleep of the thumb, fingers 4 & 5 and right leg with foot.
		47F	1 day	Unknown	Unknown	Muscular weakness Facial paralysis Ageusia Hypoaesthesia Dry eye Eye pain Paraesthesia Sensory loss Bell's palsy Herpes zoster Ear inflammation C-reactive protein increased White blood cell count increased Fine motor skill dysfunction Visual impairment	Guillain-Barré syndrome Headache Myalgia Arthralgia Fatigue Paralysis Loss of proprioception	Concomitant medications: Nuvaring, Fluoxetine

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
						Nervous system disorder Neuropathy peripheral Hypertension Headache		
4.1(b) [redacted]	[redacted]	Unk, M	< 2 weeks (est)	Unknown	Unknown	Muscular weakness Hypoaesthesia	Not Reported	

Five (5) cases were classified in the table above. These cases involved 1 male of unknown age, and 4 females with age range 30-51 years. One (1) report, 4.1(b) [redacted] co-reported with Bell's palsy in an individual with a history of GBS, which is known to cause paraesthesia. The remaining ICSRs are not suggestive of any specific context or etiology.

Table 15: Summary Table of Co-Reported Miscellaneous Events

Presented in the table below are cases with the event of interest, co-reported with miscellaneous events.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		23F	<2weeks (est)	Not resolved	55 days, ongoing	Dysgeusia, Hypoaesthesia, Neck pain, Paraesthesia, Throat tightness	Not reported	23-year-old F, who experienced dysgeusia, hypoaesthesia, neck pain, paraesthesia and throat tightness after primary vaccination. The events were reported as ongoing.
		36F	< 4 weeks (est)	Not resolved	2 months (est)	Coordination abnormal, Hyperaesthesia Mobility decreased Neuralgia Paraesthesia Sleep disorder Speech disorder	Not reported	
		26M	12 days	Not resolved	Unknown	Paraesthesia, Headache	Mite Allergy	2 weeks approx. after vaccination he experienced headache (on the right half of the head), tingling and numbness in both index finger.
		35F	Unknown	Not resolved	Unknown	Paraesthesia, Pain in extremity, Arthralgia	Methylenetetrahydrofolate reductase gene mutation	food allergy, methylenetetrahydrofolate reductase gene mutation and 8 weeks legs paralyzed with severe painful swellings at 3rd HPV vaccination. On 23-MAR-2022, after vaccination, experienced numbness in both hands and taste loss. Not Recovered. Chicken egg protein allergy, Vaccination reaction at 3rd HPV vaccination, 8 weeks legs paralyzed with severe painful swellings
		45F	2 days	Not resolved	Unknown	Paraesthesia, Pruritus	Seasonal allergy	
		19M	2 days	Not resolved	< 85 days	Axillary pain, Contusion, Lymphadenopathy, Arthralgia, Hypoaesthesia	Upper limb fracture, COVID-19	Numbness
		68F	Unk	Not resolved	<3 weeks (est)	Sleep disorder, Fatigue, Paraesthesia	Not reported	
		33F	<2 weeks (est)	Not resolved	Unknown	Vertigo, Fatigue, Headache, Paraesthesia	COVID-19	.

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		35F	<2 weeks	Not resolved	Unknown	Hypoacusis, Tinnitus, Migraine, Fatigue, Headache, Paraesthesia	Not reported	
		26M	13 days	Not resolved	50 days	Headache, Paraesthesia	Mite Allergy	2 weeks approx. after vaccination he experienced headache (on the right half of the head), tingling and numbness in both index fingers.
		41F	0 day	Not resolved	Unknown	Paraesthesia, Limb discomfort, Lymphadenopathy, Injection site pain	Not Reported	On same day after vaccination, she experienced tingling in hands and localized tingling. 2-3 days after vaccination- pulling in the left chest area and pain in the armpit, a small lump.
		47F	0 day	Not resolved	Unknown	Back pain, Flank pain, Burning sensation Chills, Pain in extremity	COVID-19, Contrast media allergy, Methylenetetrahydrofolate reductase gene mutation Ischaemic stroke, Myocarditis, Pleurisy Drug intolerance	Pain and burning on the back and the left side Concomitant medications : Daparox [Paroxetine Hydrochloride] Bisoprolol Cardioaspirin Delorazepam
		58F	1 day	Not resolved	40 days	Herpes zoster, Hypoaesthesia, Arthropathy, Dysaesthesia	Not reported	On CT scan, presence of white matter hypodensity in frontal subcortical area with hypoesthesia [and thigh and buttock dysesthesia with functional impotence].
		21F	< 4 weeks (est)	Not resolved	Unknown	Heavy menstrual bleeding, Menstrual disorder, Menstruation irregular, Paraesthesia, Injection site pain	Not reported	
		Unk, F	< 2 weeks (est)	Not resolved	26 days and not resolved (est)	Pruritus, Paraesthesia, Injection site pain	Not reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		33F	< 2 weeks (est)	Not resolved	3 months (est)	Administration site nerve damage, Burning sensation, Pain in extremity, Pruritus, Product administered at inappropriate site, Hypoaesthesia, Paraesthesia	Not reported	
		31M	46 days (est)	Not resolved	37 days, ongoing	Lymphadenopathy, Feeling abnormal, Somnolence, Injection site reaction, Paraesthesia	Not reported	
		33F	46 days (est)	Not resolved	37 days, ongoing	Pruritus, Nausea, Vomiting, Hypoaesthesia, Paraesthesia	Not reported	
		36F	Day 0	Not resolved	61 days	Ageusia, Hypoaesthesia	Methylenetetrahydrofolate reductase gene mutation	numbness in both hands
		38M	0 days	Not resolved	NA	Hypoventilation, Cough, Hypotonia, Influenza, Burning sensation	Gastrointestinal stromal tumour	remission, today (day 2 after vaccine) lasting problems. Burning sensation in upper lung
		Unk M	1 day	Not resolved	Not reported	Hypokinesia Bell's palsy Hypoaesthesia Eye disorder	Not Reported	Hypoaesthesia facial
		Unk F	2 days	Not resolved	NA	Postmenopausal haemorrhage, Galactorrhoea, Hypoaesthesia	Not Reported	Numbness
		50F	<2weeks (est)	Not resolved	44 days	Burning sensation, Paraesthesia, Pruritus	Not Reported	

MER #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		54M	< 5 weeks (est)	Ongoing	2 months (est)	Neuralgia, Injection site reaction, Hypoaesthesia	Not reported	
		50F	< 1 month (est)	Ongoing	29 days, ongoing	Essential tremor, Arthralgia, Hypoaesthesia	Not reported	
		43F	68 days (est)	Ongoing	23 days, ongoing	Anosmia, Asthenia, Dysgeusia, Dyspepsia, Migraine, Nasopharyngitis, Pain, Pain in extremity, Chills, Arthralgia, Malaise, Nausea, Hypoaesthesia	Not reported	
		58F	Day 0	Ongoing	68 days	Abdominal discomfort, Food intolerance, Abdominal distension, Abdominal distension, Eructation, Hyperaesthesia, Nausea	Allergic reaction to excipient, Allergy to metals, Rash, Cross sensitivity reaction, Asthma	Hyperaesthesia (sensitive to pressure) on day 0.
		35F	<1 month (est)	Recovered	<1 month and 17 days (est)	Hypotension, Paraesthesia	Not reported	
		62M	44 days (est)	Recovered	39 days (est)	Disturbance in attention, Feeling abnormal, Neck pain, Pain in extremity, Fatigue, Paraesthesia	Not Reported	
		42M	< 2 weeks (est)	Recovering	< 18 days	Confusional state, Back pain, Disturbance in attention, Headache, Paraesthesia	Not Reported	
		62M	< 1 week (est)	Recovering	3 months, recovering (est)	Bell's palsy, Paraesthesia, Pruritus	Not Reported	No reactions after previous vaccine. Tingling occurred in right nostril, top right lip, then itchy nose and throat. Took

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
								antihistamine. Then next morning spread to right side of nose. Then right face became numb then a facial droop was present.
4.1(b)		34F	1 day	Recovering	<1 month	Hyperaesthesia, Feeling hot, Hyperhidrosis, Lymphadenopathy Chills Arthralgia	Not Reported	Improvement of symptoms on the 3rd day.
		23F	Unk	Resolved	1 month	Speech disorder, Cognitive disorder, Confusional state, Dyspnoea, Hyperhidrosis, Paraesthesia	Not reported	Concomitant medication: Estelle 35 ED
		28F	Same day	Resolved	1 day	Limb discomfort, Paraesthesia, Dyspnoea, Cough, Influenza, Lymphadenopathy, Injection site pain, Fatigue	Formaldehyde allergy, Autoimmune thyroiditis	On the same day after vaccination she, experienced paraesthesia in the arm of the injection site and limb discomfort. 1 day after vaccination -dyspnoea when exercising, tightness in the chest, injection site pain, cough, irritable cough when exercising (stair running), fatigue and flu symptoms, 8 days after vaccination - swollen lymph nodes. Visited her doctor due to flu-like symptoms which subsided after a week. The remaining symptoms completely disappeared after 3 weeks.
		41F	Day 0	Resolved	3 days	Paraesthesia, Dyspnoea	Not reported	Allergy to arthropod bite, Mite allergy, Seasonal allergy, Coagulation factor V level abnormal
		48F	< 4 weeks (est)	Resolving	2, resolving (est)	Visual impairment, Eye discharge, Eye pain, Hypoaesthesia	None Reported	

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b) *medical	4.1(b)	29F	< 5 weeks (est)	Resolving	2 months (est)	Injected limb mobility decreased, Peripheral swelling, Tendonitis, Erythema, Pain in extremity, Pruritus, Burning sensation, Hypoaesthesia	Not reported	
		39M	<12 weeks (est)	Resolving	16 days, resolving	Cough, Dyspnoea, Oropharyngeal pain, Chills, Fatigue, Headache, Product colour issue, Hypoaesthesia	Not reported	
		34F	Unk	Resolving	3 days, resolving	Feeling hot, Hyperhidrosis, Lymphadenopathy, Chills, Arthralgia, Hyperaesthesia	Not Reported	Touch sensitivity increasing. Improvement of symptoms on the 3rd day.
		40F	Day 1	Resolving	unknown	Feeling hot, Oropharyngeal pain, Burning sensation	Not Reported	Burning face (like sunburn)
		53F	Day 0	Resolving	66 days and resolving	Asthenia, Hypoaesthesia, Paraesthesia, Pain in extremity, Nausea, Nausea, Injection site pain, Headache, Unevaluable event, Injection site pain	Not reported	Approximately 5 minutes of numbed face and Paresthesia on day 0.
		55F	Day 0	Resolving	78 days	Facial paralysis, Hemiparesis, Sleep disorder, Paraesthesia, Influenza like illness, Fatigue	Seasonal allergy, Dermatitis contact, Systemic lupus erythematosus	Shooting nerve pain; muscle and limb pain

MFR #	Country	Age (years), Gender	TTO	Event Outcome	Duration	PTs	Medical History	Additional Information
4.1(b)		41F	1	Same day	Not Recovered	Paraesthesia, Limb discomfort, Lymphadenopathy, Injection site pain	Not Reported	On same day after vaccination she experienced injection site pain, tingling in hands and localised tingling. 2-3 days after vaccination- pulling in the left chest area, and pain in the equilateral armpit, a small lump.
		55M	Unknown	Unknown	Unknown	Facial paralysis, Confusional state, Paraesthesia	Not reported	
		28F	1 day	Unknown	Unknown	Paraesthesia, Chills, Pruritus, Nausea	Not reported	Night after the vaccination strong nausea and chills. Numbness feeling in foot. Day following the vaccination numbness feeling from foot until knee/upper thigh

Forty-Five (45) cases are included in the table above. None of the co-reported events were consistent with the previously described classification. Three (3) ICRS are co-reported with facial paralysis and/or Bell's palsy. The remaining ICSRs are not suggestive of any specific context or etiology.

7.3 Disproportionality Statistics

An overview of disproportionality statistics for MedDRA PT: Paraesthesias became a signal of disproportionate reporting (SDR) based on EudraVigilance Data Analysis System (EVDAS) Electronic Reaction Monitoring Report (eRMR) (16-May-2022 to 31Mar2022; n=94, ROR=5.79). Below table describes other PTs that are captured in the HLT: Paraesthesias and dysaesthesias search criteria.

HLT: Paraesthesias and dysaesthesias PTs	Total Spontaneous ICSRs (n)	ROR
Burning sensation	9	1.43
Dysaesthesia	5	4.42
Hyperaesthesia	5	3.00
Hypoaesthesia	35	2.62
Paraesthesia	94	5.79
Hemiparaesthesia	2	6.13

7.4 Literature

Transient paresthesia is commonly due to inadvertent nerve compression on an arm or leg. Several diseases are characterized by paresthesia as an initial symptom. These include central and peripheral nervous system disorders, metabolic disorders, toxins, infections, rheumatologic disorders, and cancer and cancer-related disorders.[3] In a nationwide descriptive study of adverse events after vaccination with BNT162b2 mRNA COVID-19 in Mexico, transient sensory symptoms (paresthesia, dysesthesia, numbness, pinprick, tingling, or a combination thereof) were among the most frequently reported non-serious neurologic complaints. The study found a disproportionate number of neurologic events in female recipients, which the authors attributed in part to sexual dimorphism of the immune system.[4]

These mild neurological symptoms are common following administration of all types of COVID-19 vaccines.

In Mexico (data available in form of preprint) among 704 003 subjects who received first doses of the Pfizer-BioNTech mRNA COVID-19 vaccine, 6536 adverse events following immunization were recorded. Among those, 4258 (65%) had at least one neurologic manifestation, mostly (99.6%) mild and transient [5]

8 DISCUSSION

- Paraesthesia is currently not expected per the CCDS v3.0 effective date 03May2022
- Paresthesia has been reported after vaccination with Nuvaxovid and other COVID-19 vaccines
- Over 80% of ICSRs are reported form Australia and Germany
- Paraesthesia has been reported in 79% females
- The most commonly co-reported were headache (27%), fatigue (26%), dizziness (23%), chest pain (21%), pain in extremity (17%), injection site pain (16%), nausea (15%), myalgia (13%), pyrexia (12%), and chest discomfort (10%)
- Most of the Paraesthesia events following vaccination were generally mild and transient
- Time to onset was between 0 to 5 days, when known. TTO was unknown in most reports
- There were no documented treatments for the Paraesthesia
- After detailed review of all ICSRs, no potential etiological factors or trends were identified

Summary of weight of evidence for causal association:

- High frequency of occurrence with most common PT from the MedDRA search strategy were Paraesthesia n=189 and Hypoaesthsia n=64
- Disproportionality statistics of EVDAS eRMR report for Paraesthesia with ROR of 5.79 and Hypoaesthsia with ROR of 2.62, with a change status of “increasing”.

Summary of weight of no evidence for causal association:

- ICSRs analysis did not demonstrate the causality between the signal and the product, cases did not show any moving trend to support or contradict a relationship of the safety signal to the Nuvaxovid
- Clinical data from Day 0 to Day 49 demonstrated low and balanced frequency of events
- Clinical data demonstrated no SAEs across all clinical studies pre and post crossover
- Clinical data across all clinical studies utilizing SMQ showed incident rates equal to placebo or higher in placebo group for Paraesthesia and hypoaesthesia within 3 days post vaccination and through end of follow up. Prominent background trend

was not identified in the Epi or literature that was a good comparator to aid in this assessment in the signal and the Nuvaxovid

9 CONCLUSION

Based on the review of the available information, a causal association between Nuvaxovid and Paraesthesia is considered Confirmed.

10 SAFETY REVIEW TEAM SIGNAL DISPOSITION

Safety Review Team Signal Disposition

- The Australian label section 4.8 (Adverse Effects) will be updated as requested. A labeling variation was submitted.
- Routine monitoring is recommended with an update to the CCDS.

11 REFERENCES

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12 APPENDICES

APPENDIX 1 MEDDRA SEARCH TERMS

Search Terms for Potential Cases of Paraesthesia HLT: Paraesthesias and Dysaesthesias	
MedDRA PTs	**No of events**
Paraesthesia	199
Hypoaesthesia	67
Burning sensation	22
Hyperaesthesia	6
Dysaesthesia	5
Hemiparaesthesia	2

Abbreviations: Refer to Abbreviations Table
MedDRA Version [25.0]

Appendix 23: Signal Evaluation Report for Encephalitis/Encephalomyelitis

COVID-19 Vaccine (Recombinant, Adjuvanted) (NVX-COV2373)

Main Brand Names: NUVAXOVID™

SIGNAL EVALUATION REPORT: Encephalitis and Encephalomyelitis

Date of Report: 05-Aug-2022

Marketing Authorization Holder:

(NOVAVAX, Inc.)

Electronic signature approval(s) signifies that the approver approves this document as acceptable, accurate, and complete.

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LIST OF ABBREVIATIONS

Acronym	Abbreviation Definition
AE	Adverse event
BC	Brighton Collaboration
CCDS	Company Core Data Sheet
COVID-19	Coronavirus Disease of 2019
DLP	Data Lock Point
O/E	Observed versus Expected
eRMR	Electronic Reaction Monitoring Report
EVDAS	EudraVigilance Data Analysis System
ICSR	Individual Case Safety Report
IB	International Birthdate
IME	Important medical event
MA	Marketing authorization
MedDRA	Medical Dictionary for Regulatory Activities
MFDS	South Korean Health Authority
NVX	Novavax
PT	MedDRA Preferred Term
ROR	Reporting Odd Ratio
SRT	Safety Review Team
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SDR	Signal of Disproportionate Reporting
TTO	Time to onset

1 INTRODUCTION

This signal evaluation report provides a detailed analysis on the validated safety signal of encephalitis and encephalomyelitis in association with the administration of NUVAXOVID™ COVID-19 Vaccine (recombinant, adjuvanted) (NVXCoV2373; hereafter referred to as NUVAXOVID) based on the information available to Novavax, Inc. (NVX).

NUVAXOVID is a recombinant, adjuvanted protein vaccine indicated for active immunisation to prevent Coronavirus Disease-19 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals aged 18 years of age and older (authorised as COVOVAX in India and Thailand for ages > 12 and < 18 years). Further details on the mechanism of action, indications, pharmaceutical form(s), and instructions for use are presented in the Company Core Data Sheet (CCDS). The International Birth Date (IBD) of NUVAXOVID is 20-Dec-2021 in the European Union (EU).

2 WORLDWIDE MARKET AUTHORIZATION STATUS

On 20-Dec-2021, the first marketing authorization (MA) for NUVAXOVID was granted in the European Union which is considered to the be International Birthdate (IBD).

3 SOURCE OF THE SIGNAL

A signal of encephalitis and encephalomyelitis was validated on 16-Jun-2022, following a request for additional information on this AESI by the South Korean Health Authority (MFDS) following its assessment of Safety Summary Report (SSR) 2 (period covering 1-Mar-2022 to 31-Mar-2022).

A comprehensive review of safety data relevant to encephalitis and encephalomyelitis from clinical trials and the post-marketing safety database was performed to determine whether the available evidence supports/refutes a causal association between NUVAXOVID and encephalitis/encephalomyelitis.

4 BACKGROUND

Encephalitis is an acute inflammation or swelling of the brain, typically resulting from a viral infection or the body's immune system mistakenly attacking brain tissue. Viruses are the most common cause of encephalitis. They can include HSV, measles, and viruses spread by mosquitoes, ticks, and other insects. Encephalitis typically begins with a fever and headache. A person can also experience flu-like symptoms, light sensitivity, and weakness. Less common symptoms could be stiffness of neck, limbs, slow movements, and clumsiness, as well as drowsiness and cough. The symptoms rapidly worsen, and there may be seizures, confusion, drowsiness, loss of consciousness, and possibly coma. While most people with mild cases of encephalitis will recover, the disease can be life threatening. Some risk factors include children, older adults, individuals with weakened immune system and people who live in areas where mosquitoes and ticks are common. Some complications may include loss

of memory, behavioral changes, such as anxiety, epilepsy, aphasia, language, and speech problems. Treatment may include treating underlying causes and alleviating symptoms. Diagnostic evaluation may include CT scan or MRI to detect changes in brain structure or to rule out stroke, aneurysm, or tumor. Electroencephalogram (EEG) may show sharp waves in one or both temporal lobes in people with encephalitis. Lastly, lumbar puncture may be utilized to analyze cerebrospinal fluid (CSF) for elevation of protein and white blood cell levels and/or culture.

Encephalomyelitis is inflammation of the brain and spinal cord. Damage to the myelin sheath (demyelination) affects the ability of the nerves to transmit information and can potentially cause a wide range of neurological symptoms which may include arm/leg weakness, seizures, numbness or tingling, changes in mental status and vision loss; however, the specific symptoms and severity can vary between individuals.

5 EPIDEMIOLOGY

Encephalitis and encephalomyelitis are rare and potentially severe complications due to either infectious agents or autoimmunity; however, the cause is unknown in up to 40% of cases.[1] Encephalitis affects between 10-15 people per 100,000 in the US each year.[1] The rate of hospitalization with encephalitis in the US is approximately 7 cases per 100,000 people and, among encephalitis cases, mortality rates have been estimated to be between 5-15%.[2] Encephalitis incidence in the US is slightly higher among women compared with men, and risk factors for worse outcomes include older age, immunosuppression, and major comorbidities.[2,3] A population-based study in the US estimated the prevalence of infectious encephalitis to be 11.6 cases per 100,000 person-years (PY) (viral infectious encephalitis: 8.3 per 100,000 PY; non-viral infectious encephalitis: 3.3 per 100,000 PY) and autoimmune encephalitis to be 13.7 cases per 100,000 PY.[4] Incidence rates of autoimmune encephalitis were found to be increasing over time and were greater among African Americans (38.3 per 100,000 PY) compared with Caucasians (13.7 per 100,000 PY).[4]

A systematic review investigating encephalitis following COVID-19 estimated a pooled incidence of 0.22%, while the incidence rose to 6.7% among those who experienced severe COVID-19.[5] Age- and sex-specific rates of encephalitis following COVID vaccination range from 5-18 cases per 100,000 PY, but do not differ significantly between strata of age and sex.[6] At this time, there is no report on encephalitis after COVID-19 vaccination.

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) affects between 800,000 – 2.5 millions of individuals in the US.[7,8] Reported prevalence in Europe ranges from as low as 0.2% in England[9] to 2.6% in Sweden[10] and 3.6% in the Netherlands.[11] A systematic review found the average global prevalence of ME/CFS to be 0.89%, and higher in females than males.[12] Although there have not yet been direct reports on the relationship between COVID-19 and ME/CFS risk, some studies appear to suggest that COVID-19 infection might be

associated with increased ME/CFS.[13] There has not been an association of COVID-19 vaccination and encephalomyelitis found yet.[14]

6 METHODS

6.1 Search Strategy

6.1.1 Clinical Studies

The Clinical Trial data included Integrated Safety Summary (ISS) data from studies 2019nCoV-101 Part 1 as of 28JUL2021, 2019nCoV-101 Part 2 as of 11JUN2021 using MedDRA version 24.0, 2019nCoV-302 as of 04OCT2021 using MedDRA 23.1, 2019nCoV-501 as of 27OCT 2021 and using MedDRA version 23.0 and 2019nCoV-301 as of 20JAN2022 using MedDRA version 24.0. Clinical data was reviewed for reported events with any PT containing encephalitis or encephalomyelitis.

6.1.2 Post-marketing Database

The ARGUS safety database was searched with the SMQ (broad) Encephalitis and Encephalomyelitis which includes:

- MedDRA HLT of Encephalitis nonviral infectious; Encephalitis of viral origin; Encephalitis NEC
- MedDRA SMQ (Broad) of Noninfectious encephalitis

The periods covered cumulative data for post authorization reports up to 30-Jun-2022 using MedDRA version 25.0.

Note: For the analysis in this Signal Evaluation Report, the global vaccine safety database was queried for cumulative ICSR using the broad search strategy for Encephalitis and Encephalomyelitis, which differs from the narrow search strategy utilized for the Observed versus Expected (O/E) analysis.

6.2 Analysis Strategy

The Clinical Trial data was not adjudicated against a case definition.

The data retrieved from the NVX post-authorization safety database up to 30 June 2022 were reviewed utilizing broad search strategy for completeness. All serious cases retrieved were assessed to determine whether each case met the Brighton Collaboration (BC) case definition of Encephalitis and/or Encephalomyelitis and which level of diagnostic certainty was applicable. Cases meeting BC case definition Levels 1 – 3 were reviewed at the case level and in aggregate for evidence of causality, including temporal association with NUVAXOVID administration and the presence of any alternative etiologies.

7 RESULTS

7.1 Analysis of Data from Clinical Studies

The data received from clinical studies is the ISS from 2019nCoV-101 Part1, 2019nCoV-101 Part2, 2019nCoV-501, 2019nCoV-302, 2019nCoV-301 for reported events with any PT containing encephalitis or encephalomyelitis.

During the pre-crossover period, there were no events reported of encephalitis and/or encephalomyelitis in the vaccine group or in the placebo group. During the post-crossover period, there also were no events reported in the vaccine group or the placebo group.

7.2 Analysis of ICSRs from Post Market Safety Database, Observed verses Expected (O/E) Analysis and EVDAS data

As of 01-Jul-2022, the total estimated doses of NUVAXOVID administered are 1,116,930. As of 30-Jun-2022, cumulatively a total of 1976 spontaneous ICSRs were received (1796 non-medically confirmed, 180 medically confirmed), of which 513 ICSRs received follow-up with a total of 8238 AEs (853 serious unlisted AEs, 289 serious listed AEs, 3959 non-serious unlisted AEs, and 3137 non-serious listed AEs).

A total of 187 post-marketing ICSRs were retrieved that were captured in the search strategy described above. Thirty-seven (20%) out of 187 ICSRs were classified as serious, 23 by IME convention, and 9 (<5%) by hospitalisation and 26 of the 37 serious ICSRs were not medically confirmed. Most of the reports were from Australia (67%), followed by Germany (21%).

The 3 most frequently reported PTs that were captured in this broad search criteria were Lethargy (34%), Confusional state (19%), Somnolence (14%). The 5 most frequent PTs that were co-reported with Encephalitis and /or Encephalomyelitis PTs from broad search criteria were Headache (38%), Fatigue (30%), Dizziness (24%), Myalgia (21%), and Nausea (20%).

Additionally, no signals have been identified across geographic regions where equivalent exposure has occurred with NUVAXOVID. Most serious ICSRs contained limited information on medical history, concomitant medications, vaccination history, clinical details, and diagnostic testing.

A case series analysis was performed on 37 serious ICSRs and all 37 cases were assessed to determine whether each case met the Brighton Collaboration case definition of Encephalitis and/or Encephalomyelitis and which level of diagnostic certainty was applicable. None of the cases met the Brighton Collaboration case definition of encephalomyelitis. A total of 2 ICSRs shown in Table 1 met Brighton Collaboration case definition Level 3 for encephalitis based on clinical presentation of signs and symptoms with no diagnostic evidence or exam findings present. According to the Brighton collaboration the risk window for vaccine induced encephalitis or encephalomyelitis is 2-42 days post immunization; in our analysis the 2 cases

that met a level 3 BC had times to onset of 0-1 days; this time to onset in conjunction with co-reported terms is more consistent with a reactogenic event compared to encephalitis and did not fall within the risk window for vaccine-induced encephalitis. Further, the reported events were consistent with reactogenicity. Thus, there is insufficient data to support the causality between the signal and NUVAXOVID.

Table 1: Two ICSRs that Met Brighton Collaboration Case Definition

Case Number	Age Years/ Sex	Time to Onset (Days)	Reported PTs	BC Level of Certainty	BC Rationale	Case Summary Causality Assessment
4.1(b) [redacted]	39/F	0	Confusional state, Vaccination site haematoma, Exercise tolerance decreased, Asthenia, Arrhythmia, COVID-19 immunisation, Hypomenorrhoea, Sinus node dysfunction, Dyspnoea Pulmonary pain, Tachycardia, Myokymia, Palpitations, Influenza like illness, Pyrexia, Headache, Fatigue	3	Confusion, Asthenia, Pyrexia.	Dose 2 on 15-Mar-2022. On 15-Mar-2022, 1 day after vaccination, the vaccinee experienced confusion, pyrexia, headache, flu-like symptoms, sinus node dysfunction, dyspnoea, revaccination with a different COVID-19 vaccine, pulmonary pain, tachycardia, fatigue and myokymia. There is no confirmatory diagnostic evidence supporting a diagnosis of encephalitis (BC level 3); the onset of the reported event is inconsistent with the causal association of vaccine-induced encephalitis which is -2-42 days post vaccination. The symptoms which indicate a Level 3 assessment are Pyrexia and Asthenia, which are specifically consistent with reactogenicity. Additionally, the case is confounded by revaccination of a different covid-19 vaccine one day after vaccination.
4.1(b) [redacted]	50/F	1	Loss of consciousness, Syncope, Asthenia, Chills, Pyrexia, Nausea, Vomiting, Headache	3	Loss of consciousness, Weakness generalised, Pyrexia (38.2 °C), Syncope.	Dose 1 on an unspecified date and dose 2 on 13-APR-2022. On 14-APR-2022, experienced weakness generalised, pyrexia with 38.2 °C and chills. 1 days after receiving vaccination, experienced syncope, headache, loss of consciousness, nausea, and vomiting. There is no confirmatory diagnostic evidence supporting a diagnosis of encephalitis (BC level 3); the onset of the reported event is inconsistent with the causal association of vaccine-induced encephalitis which is 2-42 days post vaccination. Further,

						the symptoms which indicate a Level 3 assessment are Pyrexia and Weakness generalised, which are specifically consistent with reactogenicity.

O/E is routinely performed and monitored for this AESI. One non-medically confirmed report met the inclusion criteria for the observed count and the crude observed rate as reported, showed a decrease when compared to the expected rate with a non-statistically significant RR of 0.45 (95% CI: 0.01 – 2.51). When assuming 50% underreporting, the results were non-statistically significant with an RR of 0.90 (95% CI: 0.03 – 5.03). When assuming 75% underreporting, the observed rate was higher than the expected rate but non-statistically significant with an RR of 1.81 (95% CI: 0.05 – 10.06). No signal requiring validation has emerged from the O/E results up to 30 June 2022.

Furthermore, the AESI of encephalitis, encephalomyelitis has not been identified as a safety observation requiring validation within the EudraVigilance Data Analysis System (EVDAS) Electronic Reaction Monitoring Report (eRMR). The most current period available during this analysis was of 16 through 30-Jun-2022 (n=1 reports, ROR of 3.51) with status of SDR as "no".

8 CONCLUSION

In clinical data there were no events reported of encephalitis and/or encephalomyelitis in the vaccine group or in the placebo group.

In post authorization data as of the data cut of 30-June-2022 with broad search, two cases met the BC case definition of encephalitis Level 3, based on clinical presentation of signs and symptoms. However, these cases had a low level of diagnostic certainty and time to onset for these signs and symptoms were consistent with reactogenicity rather than an encephalitis diagnosis.

The signal of encephalitis and /or encephalomyelitis is not confirmed based on a comprehensive review of the available evidence that does not support a causal association between NUVAXOVID and encephalitis and/or encephalomyelitis.

9 SAFETY REVIEW TEAM SIGNAL DISPOSITION

On 05-Aug-2022, the Safety Review Team concluded that the signal of encephalitis and/or encephalomyelitis is refuted.

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11 APPENDICES

MedDRA version 25.0 PTs pulled into the Encephalitis, Encephalomyelitis Broad SMQ which included: HLT of Encephalitis nonviral infectious; Encephalitis of viral origin, Encephalitis NEC, SMQ (Broad) of Noninfectious encephalitis as of 30-Jun-2022:

MedDRA PT terms	Lethargy	63	33.7%
	Confusional state	35	18.7%
	Somnolence	27	14.4%
	Musculoskeletal stiffness	13	7.0%
	Dysphagia	9	4.8%
	Memory impairment	8	4.3%
	Loss of consciousness	8	4.3%
	Disorientation	7	3.7%
	Apathy	5	2.7%
	Cognitive disorder	5	2.7%
	Speech disorder	5	2.7%
	Sensory disturbance	4	2.1%
	Facial paralysis	4	2.1%
	Hypersomnia	4	2.1%
	Seizure	3	1.6%
	Dysarthria	3	1.6%
	Aphasia	3	1.6%
	Hemiparesis	2	1.1%
	Paralysis	2	1.1%
	Paresis	2	1.1%
	Coordination abnormal	2	1.1%
	Agitation	2	1.1%
	Febrile convulsion	1	0.5%
	Visual field defect	1	0.5%
	Clonic convulsion	1	0.5%
	Dysstasia	1	0.5%
	Irritability	1	0.5%
	Unresponsive to stimuli	1	0.5%
	Listless	1	0.5%
	Affect lability	1	0.5%
	Sluggishness	1	0.5%
	Noninfective encephalitis	1	0.5%
	Nystagmus	1	0.5%
	Ataxia	1	0.5%
	Facial paresis	1	0.5%
	Mental impairment	1	0.5%
	Hypertonia	1	0.5%

Appendix 24: Signal Evaluation Report for Chest Pain/Chest Discomfort

SAFETY SIGNAL EVALUATION REPORT FOR

Chest Pain and Chest Discomfort with Use of NUVAXOVID™ DISPERSION FOR INJECTION COVID-19 VACCINE (RECOMBINANT, ADJUVANTED) (NVX-COV2373)

Date of Report: 09 Aug 2022

Marketing Authorization Holder:

(NOVAVAX, Inc.)

Electronic signature approval(s) signifies that the approver approves this document as acceptable, accurate, and complete.

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LIST OF ABBREVIATIONS

Acronym	Abbreviation Definition
AE	Adverse Event(s)
AESI	Adverse Events of Special Interest
BC	Brighton Collaboration
CCDS	Company Core Data Sheet
DLP	Data lock point
EKG	Electrocardiogram
EU	European Union
GP	General practitioner
HLT	High Level Term
ICSR	Individual Case Safety Report
LP	License Partner
MedDRA	Medical Dictionary for Regulatory Activities
N/A	Not applicable
NVX	Novavax
O/E	Observed vs. Expected
PI	Product Information
PT	Preferred Term
PVP	Pharmacovigilance Plan
RMP	Risk Management Plan
SMC	Signal Management Committee
SMQ	Standardised MedDRA Query
SSR	Summary Safety Report
UNK	Unknown

1 INTRODUCTION

This signal evaluation report provides a detailed analysis on the validated safety signal of chest pain and chest discomfort in association with the administration of NUVAXOVID™ COVID-19 Vaccine (recombinant, adjuvanted) (NVX-CoV2373; hereafter referred to as NUVAXOVID) based on the information available to Novavax, Inc. (NVX).

NUVAXOVID is a recombinant, adjuvanted protein vaccine indicated for active immunisation to prevent Coronavirus Disease-19 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals aged 18 years of age and older (authorised as COVOVAX in India and Thailand for ages ≥ 12). Further details on the mechanism of action, indications, pharmaceutical form(s), and instructions for use are presented in the Company Core Data Sheet (CCDS). The International Birth Date (IBD) of NUVAXOVID is 20-Dec-2021 in the European Union (EU).

2 SOURCE OF THE SIGNAL

A signal of chest pain was validated on 15-Jun-2022 after a request was received from Health Canada pursuant to their assessment of the 3rd monthly SSR (period covering 01-May-2022 to 31-May-2022). In addition, chest pain and chest discomfort were identified as a signal during electronic Reaction Monitoring Report (eRMR) review: chest pain (n= 86, Reporting Odds Ratio [ROR]=4.93) and chest discomfort (n=32, ROR=2.79).

To evaluate and further characterize this signal, a comprehensive review of the safety data relevant to chest pain and chest discomfort from clinical trials and the post-marketing safety database was performed.

3 BACKGROUND

3.1 Background Related to Chest Pain and Chest Discomfort

Chest pain/discomfort are non-specific symptomatic terms representing a broad spectrum of possible pathologies, ranging from acute life-threatening injury to benign transient sensations. Pain can arise from any of the internal organs enclosed within chest wall such as the heart and major vessels, the lungs and bronchi, and the esophagus or externally from ribs and muscles of the rib cage. Chest pain can be referred from extra-thoracic structures that share spinal cord segments (e.g. gall bladder), or as functional pain that cannot be traced to specific organ tissue.

The most common causes of chest pain in the primary care population are chest wall pain (20 to 50 percent), reflux esophagitis (10 to 20 percent), and costochondritis (13 percent) (McConaghy 2022). Life-threatening causes of chest pain include, but are not limited to myocardial infarction, aortic dissection, pulmonary embolus, tension pneumothorax, pericardial tamponade and mediastinitis (esophageal rupture) (Hollander, 2022).

3.2 Labeling

Chest pain and chest discomfort are not labeled events as per the CCDS v5.0.

4 EXPOSURE DATA

4.1 Cumulative Subject Exposure in Clinical Trials

Cumulatively, 30,075 adult subjects were administered NUVAXOVID and 19,875 were administered placebo in the integrated analysis set.

Subjects were exposed in the following clinical trials:

- 2019nCoV-101 Part 1
- 2019nCoV-101 Part 2
- 2019nCoV-301
- 2019nCoV-301 Adolescent Expansion
- 2019nCoV-302
- 2019nCoV-501

4.2 Cumulative Exposure Data from Post-Authorization Experience

Exposure data are derived from administration records and distribution data. Table 1 below lists regional sources of administration and distribution data, including cut-off dates. Administration data stratified by region are provided in Table 2. Distribution data are provided for all regions that received NUVAXOVID and COVOVAX, including some regions where administration data are also available.

Table 1: Administration and Distribution Source Data by Country

Country	Administration Data Source	Administration Data Cut-Off Date	Distribution Data Source	Distribution Data Cut-off Date
Countries Included in O/E Analysis				
Australia[a]	COVID19VaccineData@Health.gov.au	26-Jun-2022	Novavax Global Sales	01-Jul-2022
Canada[a]	https://health-infobase.canada.ca/covid-19/vaccination-coverage/#a6	30-Jun-2022[c]	Novavax Global Sales	01-Jul-2022
EU[a]	https://www.ecdc.europa.eu/en/publications-data/data-covid-19-vaccination-eu-eea	30-Jun-2022[c]	Novavax Global Sales	01-Jul-2022
Japan[a]	Takeda Pharmaceutical Company	30-Jun-2022	Takeda Pharmaceutical Company	01-Jul-2022

Table 1: Administration and Distribution Source Data by Country

Country	Administration Data Source	Administration Data Cut-Off Date	Distribution Data Source	Distribution Data Cut-off Date
New Zealand[a]	New Zealand Ministry of Health (NZ MoH) provided by license partner (LP), Biocelect, via Biointelect	31-May-2022	Novavax Global Sales	01-Jul-2022
Singapore[aa]	N/A	N/A	Novavax Global Sales	01-Jul-2022
Countries Not Included in O/E Analysis				
Bangladesh[b]	http://103.247.238.92/webportal/pages/covid19-vaccination-update.php	N/A	SIIPL's SSR 09 (01-May-2022 to 31-May-2022)	N/A
India[b]	N/A	04-Jul-2022	SIIPL's SSR 09 (01-May-2022 to 31-May-2022)	N/A
Indonesia[b]	N/A	N/A	SIIPL's SSR 09 (01-May-2022 to 31-May-2022)	N/A
Philippines[b]	https://www.fda.gov.ph/list-of-fda-issued-emergency-use-authorisation/	N/A	SIIPL's SSR 09 (01-May-2022 to 31-May-2022)	N/A
Thailand	N/A	N/A	SIIPL's SSR 09 (01-May-2022 to 31-May-2022)	N/A
South Korea[a]	https://www.kdca.go.kr/board/board.es?mid=a20501020000&bid=0015&list_no=718699&cg_code=C01&act=view&nPage=1	30-Jun-2022	SK Bio Distribution Data	01-Jul-2022
UAE[a]	N/A	N/A	Novavax Global Sales	N/A
UK[a]	Communication from Vaccine Delivery Team Gov.UK/beis	N/A	Novavax Global Sales	N/A
Taiwan	N/A	N/A	Novavax Global Sales	01-Jul-2022

Abbreviations: Refer to List of Abbreviations.
Note: Not Applicable (N/A) indicates source data was unavailable for a given territory or region.

[a] NUVAXOVID
[b] COVOVAX
[c] Cut-off date is not reported by Canada and European Center for Disease Prevention and Control (ECDC). Date presented for Canada and EU in this table is the date of extraction.

Cumulatively, 1,071,963 NUVAXOVID doses were administered in Australia, Canada, EU, Japan, New Zealand, and South Korea and a total of 55,538,630 NVX-CoV2373 doses (46,318,630 NUVAXOVID and 9,220,000 COVOVAX doses) were distributed globally (Table 2).

Table 2 Cumulative Exposure Data (Distributed and Administered) from Post-Authorisation Experience Presented by Region/LP

Region / LP	Total Doses Administered[a]	Total Doses Distributed[a]
Australia (Biocelect Pty Ltd.)[b]	159,866	6,864,600
Canada (NVX)[b]	6,815	3,238,100
EU (NVX)[b]	298,543	27,980,190
India[c]	NA	12,000
Indonesia (SIIPL)[c]	NA	9,008,000
Japan (Takeda)[b]	31,102	3,641,380
New Zealand (Biocelect New Zealand Ltd.) [b]	3,904	1,251,600
Singapore (PharmaEng Technology Pte Ltd) [b]	NA	504,000
South Korea (SK Bioscience)[b]	571,733	2,334,760
Taiwan [b]	NA	504,000
Thailand (SIIPL)[c]	N/A	200,000
NUVAXOVID Total	**1,071,963**	**46,318,630**
COVOVAX Total	**N/A**	**9,220,000**

Abbreviations: Refer to List of Abbreviations.
Note: Data Sources and cut-off dates are presented in Table 1.
[a] Data presented as recorded.
[b] NUVAXOVID
[c] COVOVAX

5 METHODS

5.1 Search Strategy

5.1.1 Post-Authorization Data

The following search strategy was used to retrieve relevant safety data. A cumulative search of the ARGUS post-authorization safety database was performed with the following MedDRA Preferred Terms (PTs) with a DLP of 30 June 2022:

- Chest pain
- Chest discomfort

5.1.2 Clinical Studies

The clinical trial database was reviewed for PTs of Chest pain and Chest discomfort. The search included unblinded data from Day 0 to 49 from Studies 2019nCoV-101 Part1 as of 28JUL2021 (MedDRA version 24.0), 2019nCoV-101 Part2 as of 11JUN2021 (MedDRA version 24.0), 2019nCoV-302 as of 27JUL2021 (MedDRA version 23.1), 2019nCoV-501 as of 27OCT2021 (MedDRA version 23.0), and 2019nCoV-301 as of 17FEB2022 (MedDRA version 24.0).

5.2 Analysis Strategy

5.2.1 Case Review

All cases retrieved from post-authorization data were reviewed with a focus on cases that were serious due to criteria of hospitalization, disability and/or life-threatening.

5.2.2 Causality Assessment

Cases with seriousness criteria of hospitalization, disability and/or life-threatening were reviewed at the case level and in aggregate for evidence of causality, including temporal association with NUVAXOVID administration and the presence of any alternative etiologies.

6 RESULTS

6.1 Analysis of Data from Clinical Studies

A summary of clinical trial cases of chest pain and chest discomfort is shown in Table 3, below. No treatment group difference was noted.

Table 3: Chest Pain and Chest Discomfort*

Summary of Unsolicited Adverse Events Reported from Day 0 to 49 (28 Days Post Dose 2)(Integrated Data from Studies 2019nCoV-101 Part1/ 2019nCoV-101 Part2/ 2019nCoV-301 / 2019nCoV-302 / 2019nCoV-501)

SOC: General disorders and administration site conditions	**Vaccine** (n, %, 95% CI) N= 30075	**Placebo** (n, %, 95% CI) N= 19875	**Risk difference** (Vaccine-Placebo) (%,95% CI)
PT: Chest discomfort	23 (0.08)	12 (0.06)	0.03 (-0.02, 0.08)
PT: Chest pain	11 (0.04)	11 (0.06)	-0.03 (-0.07, 0.02)

*PTs Chest Pain and chest discomfort

Note: Risk difference and its Confidence Intervals (CIs) are computed from Mantel-Haenszel Standardized Risk Estimates and 95% normal confidence limits with the stratification by study, while individual group statistics are not adjusted by strata.

6.2 Analysis of Individual Case Safe Reports from Post Authorization Safety Database

6.2.1 Overview of Cases Retrieved

Cumulatively, there were 298 ICSRs of chest pain and/or chest discomfort reported, with a majority of events experienced within 5 days of vaccination, and a majority reported from Australia. The report characteristics and demographics are summarised in Table 4 and

Table 5 respectively. There were 25 ICSRs (8.4%) with a seriousness criterion of hospitalisation, life threatening, or disability (not including additional cases that were serious by convention due to IME criteria). Twelve of those ICSRs were associated with reports of myocarditits and/or pericarditis. All cases that met BC criteria were discussed further in SSR #05 in the relevant sections. The details of the remaining 13 serious ICSRs are described in a case series in Table 6.

The most frequent MedDRA PTs co-reported with chest pain or chest discomfort were dyspnoea, headache, fatigue, and palpitations. Of the serious cases, the most frequently co-reported events were pericarditis, dyspnoea, and fatigue.

Table 4: Chest Pain and/or Chest Discomfort Report Characteristics (Cumulative)

		All Reports (n=298)		Serious Reports (Hospitalisation/ Life Threatening/ Disability)[a]; n=25)	
		Number of Reports	Percentage of Total Reports	Number of Serious Reports	Percentage of Total Serious Reports
Total Reports Retrieved (n)		298	100.0%	25	100.0%
Country of Incidence	Australia	222	74.5%	12	48.0%
	Germany	28	9.4%	5	20.0%
	New Zealand	15	5.0%	1	4.0%
	Italy	9	3.0%	1	4.0%
	Greece	6	2.0%	3	12.0%
	France	6	2.0%	0	0%
	Austria	3	1.0%	0	0%
	Netherlands	2	0.7%	0	0%
	Singapore	2	0.7%	1	4.0%
	Czech Republic	2	0.7%	0	0%
	Canada	1	0.3%	1	4.0%
	Belgium	1	0.3%	1	4.0%
	Finland	1	0.3%	0	0%
Seriousness Criteria	Hospitalisation	21	7.0%	21	84.0%
	Life Threatening	3	1.0%	3	12.0%
	Disability	1	0.3%	1	4.0%

Table 4: Chest Pain and/or Chest Discomfort Report Characteristics (Cumulative)

		All Reports (n=298)		Serious Reports (Hospitalisation/ Life Threatening/ Disability)[a]; n=25)	
		Number of Reports	Percentage of Total Reports	Number of Serious Reports	Percentage of Total Serious Reports
Associated PTs (n≥10 ICSRs)[b]	Chest pain	241	80.9%	21	84.0%
	Chest discomfort	101	33.9%	8	32.0%
	Dyspnoea	92	30.9%	8	32.0%
	Headache	79	26.5%	4	16.0%
	Fatigue	66	22.1%	8	32.0%
	Palpitations	59	19.8%	6	24.0%
	Dizziness	52	17.4%	5	20.0%
	Paraesthesia	45	15.1%	2	8.0%
	Pain in extremity	39	13.1%	5	20.0%
	Nausea	39	13.1%	4	16.0%
	Myalgia	38	12.8%	2	8.0%
	Pyrexia	33	11.1%	2	8.0%
	Arthralgia	29	9.7%	4	16.0%
	Lethargy	26	8.7%	2	8.0%
	Tachycardia	24	8.1%	4	16.0%
	Pericarditis	23	7.7%	9	36.0%
	Injection site pain	23	7.7%	1	4.0%
	Lymphadenopathy	20	6.7%	5	20.0%
	Malaise	16	5.4%	3	12.0%
	Migraine	16	5.4%	3	12.0%
	Abdominal pain	15	5.0%	1	4.0%
	Hypoaesthesia	15	5.0%	0	0%
	Diarrhoea	14	4.7%	2	8.0%
	Back pain	13	4.4%	3	12.0%
	Injection site reaction	13	4.4%	0	0%
	Confusional state	12	4.0%	3	12.0%
	Rash	11	3.7%	0	0%
	Hypertension	11	3.7%	1	4.0%
	Burning sensation	11	3.7%	0	0%
	Neck pain	10	3.4%	2	8.0%

Table 4: Chest Pain and/or Chest Discomfort Report Characteristics (Cumulative)

		All Reports (n=298)		Serious Reports (Hospitalisation/ Life Threatening/ Disability)[a]; n=25)	
		Number of Reports	Percentage of Total Reports	Number of Serious Reports	Percentage of Total Serious Reports
Event Latency[c]	0 - 5 Days	124	41.6%	18	72.0%
	6 - 10 Days	14	4.7%	1	4.0%
	11 - 20 Days	6	2.0%	4	16.0%
	> 21 Days	4	1.3%	1	4.0%
	UNK	153	51.3%	1	4.0%
Event Outcome (as reported in Initial Report)[c]	Not Recovered/Not Resolved	170	57.0%	12	48.0%
	Recovering/Resolving	48	16.1%	4	16.0%
	Recovered/Resolved	33	11.1%	3	12.0%
	Recovered with Sequelae	3	1.0%	2	8.0%

Abbreviations: Refer to List of Abbreviations.

[a] This tabulation does not include events that were only serious by convention due to IME criteria.

[b] A case may have more than one PT on this list.

[c] Event Latency and Event Outcome reflect the latency of the events of chest discomfort and chest pain. An ICSR may be counted twice if it contains both a PT of chest discomfort and a PT of chest pain. Event latency was determined by the Jab Date and Onset Date as reported, as well as additional information from the case narrative, when available.

Table 5: Chest Pain/Chest Discomfort Report Demographics (Cumulative)

	All Reports (n=298)		Serious Reports (Hospitalisation, Life Threatening, Disability; n=25)	
	Number of Reports	Percentage of Total Reports	Number of Serious Reports	Percentage of Total Serious Reports
Male	**106**	**35.57%**	**15**	**60.00%**
11 - 20	3	1.01%	0	0%
21 - 30	23	7.72%	4	16.00%
31 - 40	34	11.41%	7	28.00%
41 - 50	25	8.39%	3	12.00%
51 - 60	10	3.36%	1	4.00%
61 - 70	4	1.34%	0	0%
71 - 80	1	0.34%	0	0%
Adult	2	0.67%	0	0%
Elderly	2	0.67%	0	0%
UNK	2	0.67%	0	0%
Female	**188**	**63.09%**	**10**	**40.00%**

	All Reports (n=298)		Serious Reports (Hospitalisation, Life Threatening, Disability; n=25)	
	Number of Reports	**Percentage of Total Reports**	**Number of Serious Reports**	**Percentage of Total Serious Reports**
11 - 20	1	0.34%	0	0%
21 - 30	32	10.74%	4	16.00%
31 - 40	49	16.44%	0	0%
41 - 50	45	15.10%	3	12.00%
51 - 60	32	10.74%	1	4.00%
61 - 70	12	4.03%	0	0%
71 - 80	6	2.01%	1	4.00%
Adult	3	1.01%	0	0%
UNK	8	2.68%	1	4.00%
UNK Gender	**4**	**1.34%**	0	0%
21 - 30	1	0.34%	0	0%
31 - 40	2	0.67%	0	0%
41 - 50	1	0.34%	0	0%

Table 6: Case Series for Serious (Hospitalisation, Life Threatening, Disability) Reports of Chest Pain/Chest Discomfort (excluding cases of Myocarditis/Pericarditis)

Case Number	Country	Age Category	Gender	Event Seriousness Criteria	TTO (Days)	Brief Case Summary
4.1(b)		UNK	Female	Disability	2	A female of unspecified age was vaccinated with Nuvaxovid on 28-Mar-2022. One day after vaccination the individual experienced shooting pain, low back pain, muscle cramp, and pain in legs. Two days after vaccination the individual experienced tummy ache and diarrhea. Three days after vaccination the individual experienced myalgia stinging arthralgia axillary lymph nodes enlarged, chest pain, muscle pain, painful arm, injection site reaction, headache, neck pain, and malaise. The events of muscle spasms, shooting pain, back pain, and pain in legs were resolved as of two days after vaccination.
		21 – 30	Male	Hospitalisation	0	A 22-year-old male was vaccinated with an unknown dose of Nuvaxovid. The individual experienced heart pain, heart fluttering, heart discomfort, heart palpitations, pain in armpit area, feeling tired, feeling weak, left wrist pain, left arm pain, and pain in left armpit area. He went to the Emergency Room and was possibly treated with Panadol and Nurofen. A chest x-ray, EKG, and blood test were performed (results are not available).
		31 – 40	Male	Hospitalisation	1	A 38-year-old male was vaccinated with his primary dose 1 of Nuvaxovid on 02-Mar-2022. On 03-Mar-2022, he experienced chest pains, shortness of breath, stabbing chest pains when large breath taken, chest pressure and discomfort, and was tired and weak and was hospitalised twice and visited his GP once.
		31 – 40	Male	Hospitalisation	1	A 35-year-old male was vaccinated with an unknown dose of Nuvaxovid. The individual experienced heart pain, headaches, pins and needles in head, earaches, and ear infection. He went to the hospital where an EKG was performed with normal results and visited a doctor who placed him on antibiotics. He has no prior history of ear infections.
		31 – 40	Male	Hospitalisation	0	A 32 year-old-male was vaccinated with a booster dose of Nuvaxovid on 23-Apr-2022. Medical history was reported as anxiety, hiatus hernia, cannabis use, and prior drug allergies to Celebrex [celecoxib] and Maxera [metoclopramide hydrochloride]. In addition, the individual also reported prior vaccination with Moderna COVID-19 [elasomeran] primary dose 1 on 14-May-2021 and primary dose 2 on 11-Jul-2021. The individual

Table 6: Case Series for Serious (Hospitalisation, Life Threatening, Disability) Reports of Chest Pain/Chest Discomfort (excluding cases of Myocarditis/Pericarditis)

Case Number	Country	Age Category	Gender	Event Seriousness Criteria	TTO (Days)	Brief Case Summary
						experienced a fever of 38.5 Celsius, shaking, chills, anxiety and chest pain following Moderna COVID-19 [elasomeran] primary dose 2 vaccination. Concomitant medications included metoprolol, Ciprolex [ciprofloxacin hydrochloride], Lexapro [escitalopram oxalate], Ativan [lorazepam] and cannabis. On 23-Apr-2022 (approximately 4 PM), the individual received a booster dose of Nuvaxovid, after receiving dose 1 and 2 of Moderna COVID-19 (elasomeran) in 2021. On 23-Apr-2022, after vaccination, the individual experienced nausea, anxiety, and afterwards, chest pain, which started 30 minutes after vaccination and lasted between 7 to 14 days, and subsequently subsided. The individual was taken to Urgent Care by ambulance approximately 3 hours following the administration of their vaccine and was admitted into hospital at approximately 7pm on 23-Apr-2022. Relevant lab tests included: Troponin (Result: "results under 3").
[redacted]	[redacted]	31 - 40	Male	Hospitalisation	5	A 36-year-old male was vaccinated with intramuscular Nuvaxovid 10 ug/mL primary dose 1 on 01-MAR-2022 and primary dose 2 on 22-Mar-2022. No medical history or comcomitant medications were reported. On 06-Mar-2022, 5 days after the first dose of the vaccine, the individual experienced chest pain (PT: Chest pain) (Serious: Hospitalisation). On 23-Mar-2022, 1 day after the second dose of the vaccine, the individual experienced exhaustion (PT: Fatigue), fatigue (PT: Fatigue) and flu-like symptoms (PT: Influenza like illness) and was hospitalised. The report described “No cardiovascular risk profile, NR, NT, athletic / - BE to rule out myocarditis and thrombosis, D dime TropT and CK MB Normal values. X-ray thorax on own initiative in the CNA without pathological alterations. Presentation to the ambulant cardiologist with TT without evidence of defects, no edema. EKG without p.B.” Medication: using Novalgin 1g IV only short lasting; Pain relief, pain with pressure left thoracic persisting.At the time of reporting, the event outcomes of fatigue was recovering/resolving and event stop date was 25-Mar-2022, influenza like illness was recovering/resolving and event stop date was 25-Mar-2022, fatigue was recovering/resolving and event stop

Table 6: Case Series for Serious (Hospitalisation, Life Threatening, Disability) Reports of Chest Pain/Chest Discomfort (excluding cases of Myocarditis/Pericarditis)

Case Number	Country	Age Category	Gender	Event Seriousness Criteria	TTO (Days)	Brief Case Summary
						date was 25-Mar-2022 and chest pain was recovered with sequelae and event stop date was 28-Mar-2022.
4.1(b)		31 – 40	Male	Hospitalisation	1	A 38-year-old male was vaccinated with primary dose 1 of Nuvaxovid. The individual had a medical history of mite allergy. The individual experienced muscle aches one day post-vaccination, noticeable heartbeat and shortness of breath two days post-vaccination, and tightness in chest, and shortness of breath three days post-vaccination. On Days 4 to 6 post-vaccination the individual reported that symptoms became intermittently stronger and weaker, with stabbing pain in his chest.
		41 – 50	Female	Hospitalisation	1	A 42-year-old female was vaccinated with primary dose 1 of Nuvaxovid on 11-Mar-2022. The individual has a medical history of aspirin allergy. On 12-Mar-2022, 1 day after vaccination, the individual experienced chest tightness (pressure in the chest), sensory disturbance and breathing difficulty. At the time of reporting, the outcome of Chest discomfort, Dyspnoea and Sensory disturbance was not recovered/not resolved.
		21 - 30	Female	Hospitalisation	2	A 24-year-old female was vaccinated with primary dose 1 of Nuvaxovid on an unspecified date. The individual had previously participated in a non-Novavax study, SafeVac 2.0. On 06-MAR-2022, after vaccination, the individual experienced injection site swelling, malaise, dizziness, injection site swelling, injection site pain, headache, diarrhoea, injection site itching, injection site pain, fatigue, headache, and general body pain. On 08-Mar-2022, the individual experienced malaise, nausea, pyrexia, dizziness, cardiac pain, diarrhoea, injection site swelling, injection site pain, fatigue, chest pain, headache, and swollen lymph nodes. On 10-Mar-2022, the individual experienced breast pain, injection site swelling, malaise, vaccination site discolouration, breathing difficult, arthralgia, dizziness, axillary lymph nodes enlarged, myalgia, fatigue, headache, cardiac pain, tachycardia, lymph nodes cervical swollen, and injection site pain. On 18-Mar-2022, the individual experienced headache, dizziness, fatigue, myalgia, malaise, pyrexia, and chills. At the time of reporting, all events were not recovered/not resolved.

Table 6: Case Series for Serious (Hospitalisation, Life Threatening, Disability) Reports of Chest Pain/Chest Discomfort (excluding cases of Myocarditis/Pericarditis)

Case Number	Country	Age Category	Gender	Event Seriousness Criteria	TTO (Days)	Brief Case Summary
4.1(b)		51 – 60	Female	Life Threatening	0	A 53-year-old female was vaccinated with Nuvaxovid (reported as "second dose") on 23-Mar-2022. Medical history included intracranial aneurysm (twice), hypertension, and tobacco user. The individual was previously vaccinated with Sinopharm in 4.1(b) . Post-vaccination, on the same day, the individual experienced, arrhythmia, severe back pain, and severe chest pain. One day post-vaccination, the individual experienced permanent intense “dysosmia (blood - mold)”. The source documentation presented conflicting information on whether the arrhythmia, chest pain, and back pain had resolved four days post-vaccination.
		41 - 50	Female	Hospitalisation	0	A 42-year-old female was vaccinated with primary dose 1 of Nuvaxovid on 20-Apr-2022. Medical history was reported as post-acute COVID-19 syndrome, tobacco user (2002), uterine leiomyoma, ovarian cyst, COVID-19 (12-Jun-2021), and thyroid mass. No concomitant medications were reported. On 20-Apr-2022, after vaccination, the individual experienced pain in skull, dizziness, cold sweat, sharp chest pain, and neck pain left for 2 hours and tachycardia. On 21-Apr-2022, the individual experienced breathing difficult, back pain, injection site swelling, fever 38 degree Celsius, and chest pain. On 22-Apr-2022, the individual experienced sleeping for 26 hours continuously. On 24-Apr-2022, the individual experienced migraine, abnormal breathing, nausea, fatigue extreme, feverish, and sleeping for over 12 hours. On 26-Apr-2022, the individual experienced axillary and inguinal lymph nodes pain, axillary lymph nodes enlarged, inguinal lymph nodes enlarged, and left ear pain. At the time of reporting all events were resolved or recovering/resolving.
		51 – 60	Male	Life Threatening	59	A 58-year-old male was vaccinated with primary dose 1 of Nuvaxovid on 05-Mar-2022. On 03-May-2022, after vaccination, the individual experienced chest pain and haemoptysis. At the time of reporting, the event outcome of chest pain and haemoptysis was recovering/resolving.
		21 - 30	Female	Hospitalisation	0	A 4.1(b) female of 24 years was vaccinated with intramuscular Nuvaxovid 10 ug/mL Booster on 07-Jun-2022. Medical history included

Table 6: Case Series for Serious (Hospitalisation, Life Threatening, Disability) Reports of Chest Pain/Chest Discomfort (excluding cases of Myocarditis/Pericarditis)

Case Number	Country	Age Category	Gender	Event Seriousness Criteria	TTO (Days)	Brief Case Summary
						prior vaccinations with Pfizer-Biontech/Comirnaty Covid-19 Vaccine (Tozinameran); 08/06/2021, dose 1 after which she experienced pharyngeal swelling, dyspnoea, and pyrexia), Sinovac-Coronavac Covid-19 Vaccine (SARS-CoV-2 Vaccine (Vero Cell); 19/08/2021 and 09/09/2021 (experiencing dizziness, cough, chest discomfort, pharyngeal swelling, rash), clarithromycin and eczema (uses occasional steroid cream). On 07-Jun-2022, 10 minutes after vaccination, the individual experienced chest tightness (PT: Chest discomfort), sob; appears dyspnoeic (PT: Dyspnoea), giddiness (PT: Dizziness), throat and eye itchiness (PT: Throat irritation and PT: Eye pruritus), and allergic reaction (PT: Hypersensitivity) and was hospitalised. Relevant lab tests included: Coma scale (Result: 15; 07-Jun-2022), Blood pressure measurement (Result: 126/79 ; 07-Jun-2022), Blood pressure measurement (Result: 100/66 ; 07-Jun-2022 17:13), Blood pressure measurement (Result: 111/68 ; 07-Jun-2022 17:28), Heart rate (Result: 132 ; 07-Jun-2022), Heart rate (Result: 69 ; 07-Jun-2022 17:13), Heart rate (Result: 89 ; 07-Jun-2022 17:28), Oxygen saturation (Result: 99 percent; 07-Jun-2022), Oxygen saturation (Result: 99 percent; 07-Jun-2022 17:13), Oxygen saturation (Result: 99 percent; 07-Jun-2022 17:28) and Physical examination (Result: Nil Respiratory Distress Nil Audible Stridor Cranial Nerves Intact No Facial Swelling Mouth And Tongue Not Swollen Uvula Not Oedematous Neck Supple Heart: S1s2 Lungs: Clear Abdo: Soft, Non-Tender Nil Rash Over Whole Body. Neck- Eczema; 07-Jun-2022). Treatment given: IM Adrenaline at vaccination operations center. At the time of reporting, the event outcome of Chest discomfort, Dyspnoea, Dizziness, Throat irritation, Eye pruritus and Hypersensitivity was unknown.

7 DISCUSSION AND CONCLUSION

Overall, findings of this cumulative review suggest no apparent patterns or trends that would identify specific diagnoses beyond the chest pain/discomfort that may potentially relate to listed events or other topics under review (hypersensitivity, vaccination anxiety-related events and myocarditis/pericarditis), or would not be anticipated in the general population.

8 SAFETY REVIEW TEAM DISPOSITION

On 09 Aug 2022, the Safety Review Team concluded that the signal of chest pain/ discomfort is refuted.

9 REFERENCES

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McConaghy. Outpatient evaluation of the adult with chest pain.. In Givens J ed: UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com (Accessed 29 July 2022.)

Appendix 25: Signal Evaluation Report for Dizziness

COVID-19 Vaccine (Recombinant, Adjuvanted) (NVX-COV2373)

Main Brand Names: NUVAXOVID™

SIGNAL EVALUATION REPORT: Dizziness

Date of Report: 05-Aug-2022

Marketing Authorization Holder:

(NOVAVAX, Inc.)

Electronic signature approval(s) signifies that the approver approves this document as acceptable, accurate, and complete.

DESCRIPTION	NAME / TITLE	SIGNATURE / DATE
PREPARED BY:	4.1(b) [redacted]	4.1(b) [redacted]
APPROVED BY:	4.1(b) [redacted]	
APPROVED BY:	4.1(b) [redacted]	

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LIST OF ABBREVIATIONS

Acronym	Abbreviation Definition
AE	Adverse events
CCDS	Company Core Data Sheet
Covid-19	Coronavirus Disease of 2019
DLP	Data Lock Point
O/E	Observed versus Expected
eRMR	Electronic Reaction Monitoring Report
EVDAS	EudraVigilance Data Analysis System
IBD	International Birthdate
ICSR	Individual Case Safety Report
IME	Important medical event
MA	Market authorization
MedDRA	Medical Dictionary for Regulatory Activities
NVX	Novavax
PRAC	Pharmacovigilance Risk Assessment Committee
PT	MedDRA Preferred Term
ROR	Reporting Odd Ratio
SRT	Safety Review Team
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SDR	Signal of Disproportionate Reporting
TTO	Time to onset

1 INTRODUCTION

This signal evaluation report provides a detailed analysis on the validated safety signal of dizziness in association with the administration of NUVAXOVID™ COVID-19 Vaccine (recombinant, adjuvanted) (NVXCoV2373; hereafter referred to as NUVAXOVID) based on the information available to Novavax, Inc. (NVX).

NUVAXOVID is a recombinant, adjuvanted protein vaccine indicated for active immunisation to prevent Coronavirus Disease-19 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals aged 18 years of age and older (authorised as COVOVAX in India and Thailand for ages > 12 and < 18 years). Further details on the mechanism of action, indications, pharmaceutical form(s), and instructions for use are presented in the Company Core Data Sheet (CCDS). The International Birth Date (IBD) of NUVAXOVID is 20-Dec-2021 in the European Union (EU).

2 WORLDWIDE MARKET AUTHORIZATION STATUS

On 20-Dec-2021, the first marketing authorization (MA) for Nuvaxovid was granted in the European Union which is considered to be the International Birthdate (IBD).

3 SOURCE OF THE SIGNAL

A signal of dizziness was validated on 15-Jun-2022, following a request for additional information on this event by Health Canada following its assessment of Safety Summary Report (SSR) #3 (period covering 1-Apr-2022 to 30-Apr-2022).

A comprehensive review of safety data for the MedDRA Preferred Term (PT) of Dizziness from the clinical trials and the post-marketing safety database was performed to determine whether the available evidence supports/refutes a causal association between NUVAXOVID and dizziness.

4 BACKGROUND

Dizziness is a term used to describe a range of sensations, such as feeling faint, woozy, weak, or unsteady. The causes of dizziness are many. Vertigo, which is a subjective illusion of movement and disequilibrium, may be due to disturbances of the inner ear or areas of the brain controlling the perception of movement. Dizziness as part of a pre-syncopal or syncopal event includes a broad differential diagnosis, including vasovagal reflex, orthostatic hypotension, hypoglycemia, hypovolemia, hyperventilation, seizures, arrhythmia, intoxication and medication side effects. Dizziness is a common co-reported symptom in individuals with psychiatric disorders (10-25% of patients). Complications of dizziness may include falling and injury. Treatment of dizziness depends on the cause and symptoms.

5 EPIDEMIOLOGY

Dizziness is a relatively common medical condition encompassing a range of sensations including vertigo, lightheadedness, and loss of balance, and is closely associated with falls and accompanying injuries.[1,2] Large population surveys have found that the prevalence of dizziness among adults ranges from 15-36%.[3,4] A survey completed among US adults found that 14.8% reported experiencing dizziness within the past 12 months, representing a total of 33.4 million adult people.[1] In population surveys completed in Europe, 22.9% of adults in a German study[5] reported moderate-to-severe vertigo or dizziness and 35.6% of French respondents[4] reported some dizziness within the past year. The prevalence of dizziness has been demonstrated to increase with age, be greater among women compared with men, and be comorbid with anxiety.[3,4] Among children and adolescents in the United States (3-17 years old), the prevalence of dizziness reported over a 12-month period was 5.3% (reflecting 3.3 millions of subjects), was more common among girls (5.7%) compared with boys (5.0%), increased with age, and was higher among White Non-Hispanic respondents (6.1%) compared with all other race/ethnicity categories (4.3-4.6%).[6] Dizziness has been reported to be the most common neurological manifestation following COVID-19,[7] with a study of SARS-CoV-2 infected patients finding that 60% reported some degree of dizziness or vertigo.[8] In addition, dizziness was reported by 8.3% of healthcare workers who received the Pfizer COVID-19 vaccine.[9]

6 METHODS

6.1 Search Strategy

6.1.1 Clinical Studies

The Clinical trial data in the safety analysis set was searched for the PT of Dizziness.

The periods covered cumulative data for clinical studies 2019nCoV-101 Part 1 as of 28JUL2021, 2019nCoV-101 Part 2 as of 11JUN2021 using MedDRA version 24.0, 2019nCoV-302 as of 04OCT2021 using MedDRA 23.1, 2019nCoV-501 as of 27OCT 2021 and using MedDRA version 23.0 and 2019nCoV-301 as of 20JAN2022 using MedDRA version 24.0.

6.1.2 Post-marketing Database

The ARGUS safety database was searched for the PT of Dizziness. The period covered cumulative data up to 30-Jun-2022 using MedDRA version 25.0.

6.2 Analysis Strategy

The data received from clinical studies in the Integrated Safety Summary (ISS) from 2019nCoV-101 Part1, 2019nCoV-101 Part2, 2019nCoV-501, 2019nCoV-302, 2019nCoV-

301 with cut off dates as noted above was assessed. No adjudication against a case definition was to be performed on the results of this search strategy.

The data retrieved from the NVX post-authorization safety database up to 30 June 2022 were reviewed for the PT of Dizziness and its temporal association with NUVAXOVID administration and the presence of any alternative etiologies. No adjudication against a case definition was performed on the results.

7 RESULTS

7.1 Analysis of Data from Clinical Studies

The data received from clinical studies is the ISS from 2019nCoV-101 Part1, 2019nCoV-101 Part2, 2019nCoV-501, 2019nCoV-302, 2019nCoV-301 for reported events with any PT of Dizziness.

Unsolicited Adverse Events Reported from Day 0 to 49 (28 Days Post Dose 2) included 101 (0.34%) events of PT Dizziness in the vaccine group and 66 (0.33%) events in the placebo group.

7.2 Analysis of ICSRs from Post Market Safety Database, and EVDAS data

As of 01-Jul-2022, the total of estimated doses of NUVAXOVID administered is 1,116,930. As of 30-Jun-2022, cumulatively a total of 1976 spontaneous ICSRs were received (1796 non-medically confirmed, 180 medically confirmed), of which 513 ICSRs received follow-up with a total of 8238 AEs (853 serious unlisted AEs, 289 serious listed AEs, 3959 non-serious unlisted AEs, and 3137 non-serious listed AEs).

A total of 253 post-marketing ICSRs were retrieved that were captured in the search strategy described above. Twenty-nine (12%) of 253 ICSRs were classified as serious, with 15 (6%) considered serious due to hospitalisation. None of the 29 serious ICSRs were medically confirmed. Most of the reports were from Germany (45%) and Australia (39%). Time to onset was reported in 176 (70%) cases, occurring most commonly between day 0 and day 5. Dizziness was reported most often by females, in 70% of total events. Co-reported multi-system symptoms were frequently reported, including headache (38%), fatigue (37%) nausea (28%), dyspnoea (16%), malaise (16%), paraesthesia (16%), myalgia (16%), chest pain (15%), pyrexia (14%), tachycardia (13%). Syncope was co-reported in 8 (3%) ICSRs with time to onset of 1 to 8 days with 2 ICSRs that had resolved outcome and 1 of these ICSR had outcome resolution within 1 day of syncope onset. Hypersensitivity is listed event in current CCDS and was co-reported in 7 (<3%) ICSRs. In most cases, this constellation of co-reported symptoms may be associated with reactogenicity, or anxiety, and did not suggest a specific neurologic pattern.

Table 3 presents a case series analysis that was completed on 15 events of PT Dizziness requiring hospitalisation. Limited information was provided in most of these reports, including lack of medical history, no information on concurrent medications or vaccination history and no clinical or diagnostic details of the event. No medical treatment was reported for Dizziness. There is insufficient information to support a causal association with NUVAXOVID, and no pattern of co-reported conditions could be identified. Report characteristics are summarized in Table 1 and demographics in Table 2.

The PT Dizziness has been identified as a safety observation since meeting the EudraVigilance Data Analysis System (EVDAS) Electronic Reaction Monitoring Report (eRMR) criteria. The most current period available during this analysis was of 16 through 30-Jun-2022 (n=166 reports, ROR of 3.62) with status of SDR as "increased".

Table 1: Report Characteristics

Report Characteristics			
Dizziness: PT of Dizziness MedDRA v25.0, Cumulative to 30-Jun-2022		**n**	**%**
Total reports retrieved		253	100
Report origin	Germany	114	45.1
	Australia	99	39.1
	New Zealand	11	4.3
	Italy	9	3.6
	Austria	5	2.0
	Japan	4	1.6
	Singapore	3	1.2
	Greece	2	0.8
	France	1	0.4
	Netherlands	1	0.4
	Czech Republic	1	0.4
	Sweden	1	0.4
	Lithuania	1	0.4
	Ireland	1	0.4
Seriousness/Criteria	Total Non-serious	225	88.9
	Total Serious	29	11.5
	Fatal	0	0
	Hospitalisation	15	5.9
	Medically significant	9	3.6
	Other Serious	4	1.6
	Medically significant, Disability	1	0.4
MedDRA PT terms	Dizziness	253	100
Event latency	0-5 days	156	62
	6-10 days	9	4
	Over 10 days	11	4
Event treatment	None reported for dizziness	NA	NA
Event outcome	Not Recovered/Not Resolved	114	45
	Recovered with Sequelae	3	1
	Recovered/Resolved	44	17
	Recovering/Resolving	48	19

	Unknown	46	18

Abbreviations: Refer to List of Abbreviations.

Table 2: Demographics

Demographics		
Dizziness: Search Strategy: PT of Dizziness MedDRA v25.0, Cumulative to 30-Jun-2022		
All Reports	**n=253**	**100% of Total**
Female	**187**	**74**
14	1	0.4
20-29	14	5.5
30-39	40	15.8
40-49	48	19.0
50-59	40	15.8
≥60	17	6.7
Unknown	27	10.7
Male	**66**	**26.1**
14	0	0.0
20-29	15	5.9
30-39	14	5.5
40-49	9	3.6
50-59	14	5.5
≥60	3	1.2
Unknown	11	4.3

Abbreviations: Refer to List of Abbreviations.

Table 3: Fifteen Hospitalisation ICSRs of Dizziness

Case number	Other PTs	Dizziness Outcome	Dizziness TTO (Days)	Medical History	Brief Summary
4.1(b)	Blood bilirubin increased, Chest discomfort, Chest pain, Echocardiogram abnormal, Malaise, Mitral valve thickening, Palpitations, Pericarditis, Tachycardia	Not recovered	0	Asthma	A 23-year-old male was vaccinated with dose 1 on FEB-2022. On 17-FEB-2022, after vaccination, experienced blood bilirubin increased, chest discomfort, chest pain, dizziness, echocardiogram abnormal, malaise, mitral valve thickening, palpitations, pericarditis and tachycardia. On 17-FEB-2022, Echocardiogram had abnormal results, 50% prolapse with significant thickening of the mitral valve leaflet tip, mild to moderate regurgitation. Tests of unspecified date: DNA Antibody: 705-175 on anti-DNA-sb-blood test, Liver

					function test: 55 bilirubin and Blood test: indicated recent infection/bug.
4.1(b) [redacted]	Heart rate increased, Blood pressure increased, Chills	Not recovered	0	Not reported	An unspecified age male was vaccinated with dose 1 on 06-MAR-2022. On 06-MAR-2022, 1 day after vaccination, experienced pulse increased, light headedness, pressure blood increased, and chills.
4.1(b) [redacted]	Diarrhoea, Fatigue, Paraesthesia, Feeling abnormal, Fatigue, Disturbance	Not recovered	1	Not reported	A 43-year-old female was vaccinated with dose 1 on 01-MAR-2022. On 02-MAR-2022, 1 day after vaccination, experienced diarrhea, exhaustion, tingling in the feet and hands, concentration problems, dizziness, tiredness, fog in brain.
4.1(b) [redacted]	Nausea, Dizziness, Chills, Nausea, Chills	Recovering	1	Nickel sensitivity, Medication for nausea and cardiovascular circulation stabilization	A 59-year-old female was vaccinated with dose 2 on 23-MAR-2022. On 24-MAR-2022, 1 day after vaccination, experienced nausea, drastic dizziness, chills.
4.1(b) [redacted]	Nausea, Dizziness, Asthenia, Chills, Head discomfort	Not recovered	0	Not reported	A 34-year-old female was vaccinated with dose 1 on 03-MAR-2022. On 03-MAR-2022, reported as half an hour after vaccination experienced nausea, dizziness, debility, chills, head pressure and asthenia.
4.1(b) [redacted]	Blood pressure increased, Headache, Arrhythmia, Fatigue, Visual impairment, Nausea	Recovering	1	Not reported	A 33-year-old female was vaccinated with dose 1 on 04-MAR-2022. On 05-MAR-2022, 2 days after vaccination, experienced blood pressure increased (168/122 mmHG), headache, arrhythmia, nausea, tiredness, visual disturbance, and light headedness.
4.1(b) [redacted]	Visual impairment, Headache, Musculoskeletal chest pain, Vomiting, Arthralgia, Dyspnoea, Muscle spasms, Back pain, Skin discolouration, Arthralgia, Vaccination site pain	Not recovered	10	Psoriasis since 2021	A 69-year-old female was vaccinated with dose 1 on 10-MAR-2022. 1 day after vaccination, experienced visual disturbance with flashes in the right eye and slight colour appearances, headache, prolonged heart pressure pain, and intermittent nausea and vomiting. 11 days after vaccination, experienced painful movements in the hip area, shortness of breath after waking up, constantly recurring cramps in the toes, fingers of left hand, hip area and lower back, painful movements in the low back area, recurrent dizziness especially when laid down, when the eyes are closed, and when stood up and bent forward, risk of tipping forward, slight bluish/yellow discolouration of the skin on the inside of the arms, shoulder pain in the vaccinated arm on slight rotational movement and vaccination site pain.
4.1(b) [redacted]	Goitre, Lymphadenopathy, Chills, Headache,	Not recovered	1	Allergy to penicillin	A 57-year-old female was vaccinated with dose 1 on 10-MAR-2022. On 11-MAR-2022, 2 days after vaccination,

	Emotional distress, Anxiety, Fatigue, Myalgia, Dizziness, Sleep disorder				experienced rapid enlargement of thyroid, swollen lymph nodes, chills, headache, psychological stress, anxiety, fatigue, myalgia, dizziness, sleep disorder.
4.1(b) [redacted]	Pyrexia, Hypersensitivity, Rash, Fatigue, Limb discomfort, Swelling face, Flushing, Injection site erythema, Arthralgia	Not recovered	0	Severe allergic reaction (swelling and redness on the face, cardiovascular reaction; fever) to BioNTech/Pfizer m-RNA vaccine on 06-JAN-2021	A 34-year-old female was vaccinated with dose 2 on 01-APR-2022. Secondary suspect medications: Comirnaty dose 1 on 06-JAN-2021. On 01-APR-2022, after vaccination, experienced dizziness, pyrexia, systemic allergic reaction, rash, fatigue, dizziness, swelling of face, facial flushing, injection site redness, joint pain, and limb discomfort.
4.1(b) [redacted]	Atrial fibrillation, Paresthesia, Left ventricular failure, Myocarditis, Congestive cardiomyopathy	Unknown	0	Not reported	A 59-year-old male was vaccinated with dose 1 on 25-MAR-2022. Same day, after vaccination, experienced atrial fibrillation, tingling feet/hands, myocarditis, left ventricular insufficiency, light headedness, and dilated cardiomyopathy.
4.1(b) [redacted]	Injection site swelling, Malaise, Injection site pain, Headache, Diarrhoea, Injection site pruritus, Fatigue, Pain, Malaise, Nausea, Pyrexia, Angina pectoris, Chest pain, Lymphadenopathy, Breast pain, Vaccination site discolouration, Dyspnoea, Arthralgia, Myalgia, Tachycardia, Chills	Not recovered	1	Not reported	A 24-year-old female was vaccinated with dose 1 on an unspecified date. The individual participated in non-Novavax study SafeVac 2.0. On 06-MAR-2022, after vaccination, experienced injection site swelling, malaise, dizziness, injection site pain, headache, diarrhoea, injection site itching, fatigue, general body pain. On 08-MAR-2022, experienced nausea, pyrexia, dizziness, cardiac pain, chest pain and swollen lymph node. On 10-MAR-2022, experienced breast pain, vaccination site discolouration, breathing difficult, arthralgia, myalgia, tachycardia. On 18-MAR-2022, experienced chills.
4.1(b) [redacted]	Malaise, Headache, Nerve injury, Urticaria, Fatigue, Weight bearing difficulty, Neuralgia, Fall, Gait disturbance, Muscular weakness, Paraesthesia, Limb discomfort, Dyspnoea, Feeling hot, Nasal congestion, Nausea	Unknown	0	Cluster headaches, 2009 Stroke, Tension headache, Asthma, permanent increased pain, slightest stress triggers dizziness, reinforcement and hives on top of this, thyroid antibodies have increased extremely which indicates Hashimoto, running problems, additionally on the	A 35-year-old male was vaccinated with dose 1 on 02-MAR-2022. On 02-MAR-2022, 1 day after vaccination, experienced dizziness, and malaise. 3 days after vaccination, experienced headache, nerve damage (left-sided time almost 3 months persistent nerve damage, 24h a day headache with impulse such as electricity, no physical stress without stress hives, chronic fatigue), rash urticarial, and weight bearing difficulty. 13 days after vaccination, experienced nerve pain (running problem left, middle-class nerve pain, no stress load because then immediately dizziness and nausea and weakness in limbs which led to several

				left side paralysis, numbness	falls), fall, muscle weakness and gait disorder.
4.1(b) [redacted]	Pain, Dyspnoea, Chest pain, Neck pain, Injection site swelling, Respiration abnormal, Lymphadenopathy, Back pain, Lymphadenopathy, Sleep disorder, Fatigue, Migraine, Nausea, Ear pain, Pyrexia, Sleep disorder, Cold sweat, Lymph node pain, Tachycardia, Pyrexia	Recovering	0	Post-acute COVID-19 syndrome, tobacco user (2002), uterine leiomyoma, ovarian cyst, COVID-19 (12-JUN-2021), and thyroid mass. Does not receive any medication or contraceptives	A 42-year-old female was vaccinated with dose 1 on 20-APR-2022. On 20-APR-2022, after vaccination, experienced pain in skull, dizziness, cold sweat, sharp chest pain and neck pain left for 2 hours and tachycardia. 2 days after vaccination, experienced breathing difficult, back pain, injection site swelling, fever 38 degree C and chest pain. 3 days after vaccination, experienced sleeping for 26 hours continuously. 5 days after vaccination, experienced migraine, abnormal breathing, nausea, fatigue extreme, sleeping for over 12 hours. 7 days after vaccination, experienced axillary and inguinal lymph nodes pain, axillary lymph nodes enlarged, inguinal lymph nodes enlarged and left ear pain.
4.1(b) [redacted]	Blood pressure fluctuation, Tendoniti, Migraine, Abdominal pain, Vision blurred	Not recovered	0	Not reported	An unspecified age female was vaccinated with dose 1 on 14-MAR-2022. On 14-MAR-2022, 1 day after vaccination, experienced blood pressure fluctuation, dizziness, achilles tendinitis, migraine, abdominal pain, and hazy vision.
4.1(b) [redacted]	Chest discomfort, Dyspnoea, Throat irritation, Eye pruritus, Hypersensitivity	Unknown	0	Pfizer-Biontech/Comirnaty Covid-19 Vaccine (Tozinameran); 08/06/2021, dose 1(pharyngeal swelling, dyspnoea, pyrexia), Sinovac-Coronavac Covid-19 Vaccine (Sars-Cov-2 Vaccine (Vero Cell)); 19/08/2021 and 09/09/2021 (dizziness, cough, chest discomfort, pharyngeal swelling, rash), clarithromycin and eczema (uses occasional steroid cream)	A 24-year-old female was vaccinated with Booster on 07-JUN-2022. On 07-JUN-2022, 10 minutes after vaccination, experienced chest tightness, sob; appears dyspnoeic, giddiness, throat and eye itchiness, and allergic reaction. Tests on 07-JUN-2022: Coma scale: 15, Blood pressure (BP): 126/79, Heart rate: 132 and 69, Oxygen saturation: 99% and "Physical examination: nil respiratory distress nil audible stridor cranial nerves intact no facial swelling mouth and tongue not swollen uvula not oedematous neck supple heart: s1s2 lungs: clear abdo: soft, non-tender nil rash over whole body. Neck- eczema)". Treatment: IM Adrenaline.

Abbreviations: Refer to List of Abbreviations.

8 CONCLUSION

Overall, no safety concerns have been observed during this cumulative review of adverse event reports of PT Dizziness. Analysis of adverse events reports of dizziness in the company's global safety database did not reveal any trends or patterns suggesting a safety signal. In most cases, the constellation of co-reported symptoms may be associated with reactogenicity, or anxiety, and did not suggest a specific neurologic pattern. However, based on EVDAS data dizziness is an event frequently reported.

A causal association between NUVAXOVID and dizziness is not supported by the comprehensive review of the evidence, and the signal of dizziness is not confirmed

9 SAFETY REVIEW TEAM SIGNAL DISPOSITION

On 05-Aug-2022, the Safety Review Team concluded that the signal of dizziness is refuted.

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11 APPENDICES

Not applicable

Appendix 26: Health Authorities Requests Following Review of SSRs

Requests received from HAs (not considered as a signals) are summarised in Table 49.

Table 49: Requests from HAs Assessment Reports

No	Name of Health authority	Description of Request	PBRER Section
1	PRAC assessment report for SSR No. 03	MAH to present more details regarding reactogenicity profile of second dose and boosters	Section 15.2.2.7
2	PRAC assessment report for SSR No. 03	Analysis of AESIs and other safety topics should focus on diagnostic certainty of reported adverse events (e.g., use of Brighton Collaboration case definitions or other international accepted case definitions), TTO, age and gender distribution, duration, and outcome of AEs. If feasible risk factors and confounding factors should be assessed. TTO calculations should consider narrative and other information.	Section 15.2.1
3	PRAC assessment report for SSR No. 03	To Include “Day 0” in risk windows Where appropriate, different time windows should be used in addition to the currently defined time windows (e.g., for anaphylaxis a time window of 24 h, 48 h etc). It is well known that underreporting of ICSRs correlate with the time-to-onset of ADR symptoms with more complete reporting close to the date of vaccination and an increase of underreporting over time after vaccination. Biological plausible time windows should be considered (e.g., anaphylaxis).	Section 15.2.1
4	PRAC assessment report for SSR No. 03	The risk window for "generalized convulsions" was 1 - 42 days post-vaccination. Febrile convulsions can have TTO of "zero days" and may be excluded from the O/E calculation. MAH to include in "risk windows in general the day of vaccination" for O/E.	Section 15.2.1.6
5	PRAC assessment report for SSR No. 3	MAH to collect more clinical information on ICSRs	Ongoing
6	MHRA, SSR No. 03	Reasoning and reallocation of doses for cases reported as unknown dose of dose 3, reports as dose 1 or 2 cases for the OE analysis. The validity of recoding third doses depends on the likelihood off-label” use in each country.	Section 15.2.1
7	USG (United States Government) SSR No. 03	Include” cholecystitis” in future reports	Section 15.2.2.4
8	Health Canada SSR No. 02	Provide causality assessments of reported cases of all AESI and RMP safety concerns based on causality algorithm. AESIs should be classified based on established BC case definitions, when available.	Discussed in SSR No.06

Appendix 27: References/List of Sources of Information Used to Prepare the PBRER

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