Memo

COVID-19 Vaccine Independent Safety Monitoring Board update

Date:	07 May 2021
To:	COVID-19 Vaccine and Immunisation Programme Steering Group
Copy to:	Jo Gibbs, National Director - COVID-19 Vaccine & Immunisation Programme; Dr Ian Town, Chief Science Advisor, Dr Tim Hanlon, Group Manager Post Event/Workstream Lead - COVID-19 Vaccine & Immunisation Programme
From:	Mr John Tait, Chair – COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Information

Purpose of report

1. This memo is to provide an update on the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) and their work to date.

Background and context

2. The CV-ISMB has been established to provide expert advice around the safety of COVID-19 vaccines to CARM, Medsafe, the COVID-19 Vaccine and Immunisation Programme (CVIP) and Ministry of Health.
3. The Board has expertise from clinical medicine, general practice, microbiology and biostatistics. The Board has members who represent the voice of Māori and Pasifika, along with a lay person to represent the interests of the consumer in general. Refer to Appendix 1 for a full list of members, including area of expertise and current position.
4. The Board has a regular monthly meeting to discuss cases of note (i.e., adverse events of special interest) and where Medsafe presents an update on safety data including signals under investigation. There is also provision for ad hoc meetings where the Board can be brought together to discuss an urgent issue.

Key updates & information

5. The CV-ISMB has had three general working meetings to date (last meeting 29 April) and an ad hoc meeting (22 April) which was called by Medsafe to look at the blood clotting/bleeding effects from some of the COVID-19 vaccines reported from overseas.

Ad hoc meeting to discuss thrombosis with thrombocytopenia syndrome (TTS)

6. The purpose of the ad hoc meeting on TTS was to discuss whether (i) a similar risk has been identified in New Zealand; (ii) the Pfizer vaccine is associated with this problem; (iii) if it would be beneficial to provide information on this clotting/bleeding syndrome for the public, and in that case what communication would be needed.

7. The CV-ISMB were reassured by international experience with the Pfizer-BioNTech vaccine where there has been much wider usage and the local experience to date in New Zealand was not considered to identify a risk.

8. It was agreed that Medsafe should issue a Monitoring Communication to reassure people that Medsafe is aware of the association between TTS and the AstraZeneca and Janssen COVID-19 vaccines and that the safety of the Pfizer-BioNTech vaccine is being monitored closely in regard to this issue.

Hypersensitivity/Anaphylaxis reactions

9. The rate of reported anaphylaxis is currently ~ 8/260,000 (as at 29 April) for the CVIP while the reported rate for Comirnaty is ~3-11 cases per million. Some CV-ISMB members have expressed concern that our local anaphylaxis rate might end up being spuriously high which could undermine confidence in the CVIP.

10. The CV-ISMB agreed on the 11 March 2021, that potential anaphylaxis reports should be assessed against the Brighton Collaboration Criteria for anaphylaxis (internationally used) to determine whether a reaction constitutes anaphylaxis. For this assessment detailed information needs to be collected at the time of the event or immediately after.

11. Dr Michael Tatley, Director of Centre for Adverse Reactions Monitoring (CARM) presented the anaphylaxis tabular checklist (attached as Appendix 2) to the CV-ISMB as a proposed mechanism to evaluate reported cases of anaphylaxis for the CVIP, which was supported by the Board as a useful document.

12. The proposed checklist incorporates the Brighton criteria and discussion amongst members of the CV-ISMB was split around whether this could be made available in a paper format or whether it could be incorporated into the CIR as part of the AEFI reporting mechanism to allow capture of more detailed information for assessment.

13. CARM Medical Assessors have started to evaluate all reports where the reporter has chosen anaphylaxis and those reports where the Medical Assessor thinks that the constellation of symptoms reported warrant assessment against the Brighton Criteria for anaphylaxis, however sometimes this assessment is limited by the detail provided in the initial report and whether follow up information can be obtained in a timely manner.

Current Signals under investigation

14. Medsafe updates have been keeping the Board updated around potential safety signals under investigation, currently TTS for Janssen vaccine, myocarditis, appendicitis and herpes zoster for the Pfizer-BioNTech vaccine. Where needed additional expertise is drawn on from outside the Board (i.e. both a haematologist and cardiologist have been engaged).

Ad hoc meeting process

15. A process has been drafted to bring together the group for urgent meetings. The current prompt for an urgent meeting of the Board is:

    a. urgent issues arising internationally that could threaten the stability of the CVIP

    b. a report of a serious unexpected event where further expert advice is urgently required by CARM, Medsafe or the CVIP

16. This process has been tested once and is currently being refined to ensure that there are appropriate links for feeding information out to key stakeholders and back to the CV-ISMB.

Recommendations

It is recommended that you:

1.	note	The update of the COVID-19 Vaccine Independent Safety Monitoring Board provided in this Memo	Yes/No
2.	agree	Consideration should be given by the COVID-19 Vaccine and Immunisation Programme (CVIP) to having the anaphylaxis tabular checklist (Appendix 2) available to the reporter to allow capture of more detailed information.	Yes/No

Appendix 1

COVID-19 Vaccine Independent Safety Monitoring Board

Name	Area of Expertise	Position
Mr John Tait (Chair)	Obstetrics	Chief Medical Officer CCDHB; Consultant obstetrician and gynaecologist
Dr Nick Cutfield	Neurology	Consultant Neurologist and Clinical Lead; Senior Lecturer
Associate Professor Matt Doogue	Clinical Pharmacology; Endocrinology	Consultant physician in Clinical Pharmacology and General Medicine
Dr Kyle Eggleton	General Practice	Kaupapa Māori Medical Officer at Ki A Ora Ngātiwai; Senior Lecturer
Professor Chris Frampton	Biostatistics	Professor of Biostatistics
Dr Maryann Heather	General Practice; Pacific Health	GP at South Seas Healthcare; Senior Lecturer
Dr Tom Hills	Immunology	Chief Medical Resident, Immunology
Honorary Associate Professor Hilary Longhurst	Immunology; Pathology	Senior Medical Officer, Immunology
Professor Thomas Lumley	Biostatistics	Professor of Biostatistics
Saskia Schuitemaker	Lay person – to represent consumer interests	Coordinator, Child and Youth Mortality review Group, Waikato District Health Board
Dr Owen Sinclair, Te Rarawa	Paediatrics, Māori Health	Paediatrician WDHB
Professor Lisa Stamp	Rheumatology	Professor in Medicine; Rheumatologist
Dr Anja Werno	Microbiology; Pathology	Chief of Pathology & Laboratories, Acting Clinical Director of Microbiology, CHL; Clinical Senior Lecturer, University of Otago
Dr Enver Yousuf	General Medicine	Senior Registrar CCDHB General Medicine

Appendix 2 – Draft anaphylaxis tabular checklist documentation - Adapted from AESI Desktop Companion Guide – Anaphylaxis (SPEAC - A PROJECT FUNDED IN WHOLE BY CEPI)

Anaphylaxis Tabular Checklist for Key Case Definition Criteria and Glossary of Terms

Patient Name	NHI	CIR AE	Patient Phone

DATE	Vaccine Facility	Vaccinator Name	Vaccinator Phone

Vaccine Administered	Vaccination Time	Event Onset Time

Adrenaline Time	Adrenaline Dose	Transfer to ED (Name)	Transfer Time

Anaphylaxis Tabular Checklist for Key Case Definition Criteria

1. COURSE OF ILLNESS: must be able to check both 1.1 AND 1.2 to meet any level of certainty for anaphylaxis

☐ **1.1 SUDDEN ONSET of signs & symptoms**	☐ **1.2 RAPID PROGRESSION of signs & symptoms**
"An event that occurred unexpectedly and without warning leading to a marked change in a subject's previously stable condition"	

2. ≥ 2 body systems involved: check all symptoms/signs present by checking appropriate boxes in rows below. Ideally these should be documented in writing (E.G. AEFI report, clinical record in immunization clinic, Emergency room, or other clinical setting. Alternatively, a verbal report from a professional (R.N., Dr, Pharmacist) who witnessed the event.

Body System	B. MAJOR CRITERIA	C. MINOR CRITERIA	
SKIN **excluding hereditary angioedema*	☐ Generalized urticaria (hives) ☐ Generalized erythema ☐ Angioedema* (general or localized including lip) ☐ Generalized pruritus WITH skin rash	☐ Localized injection site urticaria ☐ Red AND itchy eyes ☐ Generalized prickle sensation ☐ Generalized pruritus WITHOUT skin rash	
RESPIRATORY (RESP)	☐ Bilateral wheeze (bronchospasm; by stethoscope) ☐ Stridor ☐ Upper airway swelling (tongue, throat, uvula, larynx) ☐ ≥ 2 indicators of respiratory distress: ☐ Tachypnea ☐ Cyanosis ☐ Grunting ☐ Chest wall retractions ☐ Increased use of accessory respiratory muscles	☐ Persistent dry cough ☐ Hoarse voice ☐ Sensation of throat closure ☐ Sneezing OR rhinorrhea ☐ Difficulty breathing WITHOUT wheeze or stridor	
CARDIO-VASCULAR (CV)	☐ Measured hypotension ☐ ≥ 3 signs of uncompensated shock: ☐ Tachycardia ☐ Capillary refill >3 seconds ☐ Reduced central pulse volume ☐ Decreased level or loss of consciousness	☐ ≥ 2 signs of reduced peripheral circulation ☐ Tachycardia ☐ Capillary refill >3 seconds ☐ Decreased level of consciousness	
GASTRO-INTESTINAL (GI)	NONE	☐ Nausea ☐ Abdominal pain	☐ Vomiting ☐ Diarrhea
LABORATORY	NONE	☐ Elevated mast cell tryptase (> upper normal limit for laboratory doing test)	

Accessory muscles	Muscles, primarily in the neck (sternocleidomastoid which elevates sternum; scalene group which elevates upper ribs) which assist but don't play a primary role in breathing. When used at rest they indicate a level of respiratory distress or increased work of breathing.
Angioedema	Areas of deeper swelling of the skin and/or mucosal tissues in either single or multiple sites which may not be well circumscribed and usually not itchy. (Reported symptoms of "swelling of the tongue" or "throat swelling" should not be documented as angioedema unless there is visible skin or mucosal swelling). NOTE: hereditary angioedema, usually with a history of recurrent episodes of swelling, should be excluded (affects 1 in 50,000)
Capillary refill time	The time required for normal skin colour to reappear after a blanching pressure is applied for 5 seconds. Usually assessed by pressing on the nail bed to cause blanching and then counting the time it takes for the blood to return to the tissue indicated by a pink colour returning to the nail. It normally takes < 3 seconds.
Cyanosis	A dark bluish or purplish discolouration of the skin and/or mucous membranes due to lack of oxygen in the blood
Dry cough	Rapid expulsion of air from the lungs and not accompanied by expectoration/sputum (a non-productive cough)
Erythema	Abnormal redness of the skin without any raised skin lesions
Generalized	Involving >1 body site – that is each limb is counted separately as is the abdomen, back, head and neck
Grunting	A sudden and short noise with each breath when breathing out
Hoarse voice	An unnaturally harsh cry in an infant or vocalisation in and adult or child
Hypotension	An abnormally low blood pressure (BP) documented by appropriate measurement. For infants and children: age specific systolic BP <3-5th percentile OR >30% decrease from that person's baseline; For adults: Systolic BP of <90mm Hg or >30% decrease from that person's baseline.
In-drawing or retractions	Inward movement of the muscles between the ribs (inter-costal), in the lower part of the neck (supra-clavicular or tracheal tug) or below the chest (sub-costal). The movements are usually a sign of difficulty with breathing which results in increased use of 'accessory respiratory muscles' (sternocleidomastoid and intercostal).
Injection site urticaria	Urticaria which is continuous with the injection site or involves other aspects of the injected limb
Localised	Involving one body site only
Loss of consciousness	Total suspension of conscious relationship with the outside world as demonstrated by an inability to perceive and respond to verbal, visual or painful stimulus
Mast cell tryptase	Inflammatory mediator released by mast cells during acute anaphylaxis. Typically levels peak between 15 and 120 minutes after onset; samples for measurement should be taken within 6 hours of onset of signs/symptoms.
Prickle sensation	An unpleasant skin sensation that provokes the desire to run and/or scratch to obtain relief
Pruritus	Itchiness
Red and itchy eyes	Redness of the whites of the eyes (sclera) with sensation that provokes the desire to rub and/or scratch to obtain relief.
Retractions	Indrawing of skin while breathing in (implies an obstruction to breathing); may be supraclavicular (above the collarbone), suprasternal (above the sternum), intercostal (between the ribs), substernal (below the sternum) or subcostal (abdomen just below the rib cage)
Rhinorrhea	Discharge of thin nasal mucus
Sensation of throat closure	Feeling or perception of throat closing with a sensation of difficulty breathing
Sneezing	An involuntary (reflex), sudden, violent, and audible expulsion of air through the mouth and nose.
Stridor	A harsh and continuous sound made on breathing in
Tachycardia	Faster than normal heart rate which varies by age – Adult >100 bpm
Tachypnoea	Faster than normal respiratory rate which varies by age – Adult >16 bpm
Urticaria	Localized redness of superficial layers of skin that is itchy, raised, sharply demarcated and transient (that is skin changes at any location are usually present for less than 12 hours)
Wheezing	A whistling, squeaking, musical or puffing sound made on breathing out

Document 1

CRITERIA FOR LEVEL OF CERTAINTY FOR MEETING BRIGHTON CASE DEFINITION OF ANAPHYLAXIS

Patient Name	NHI	CIR AE	Patient Phone

DATE	Vaccine Facility	Vaccinator Name	Vaccinator Phone

Vaccine Administered	Vaccination Time	Event Onset Time

☐ **SUDDEN ONSET of signs & symptoms** ☐ **RAPID PROGRESSION of signs & symptoms**

Level of Certainty	≥1 Skin	≥1 Respiratory	≥1 Cardiovascular	Additional Criteria needed to meet Level II or III
Level 1	☐ MAJOR	☐ MAJOR	☐ MAJOR	
	☐ MAJOR	☐ MAJOR		
	☐ MAJOR		☐ MAJOR	
Level 2	☐ MAJOR	☐ Minor		
	☐ MAJOR		☐ Minor	
	☐ MAJOR	☐ Minor	☐ Minor	
		☐ MAJOR	☐ MAJOR	
		☐ MAJOR		☐ ≥ 1 minor from skin, CVS, GI or elevated MCT
			☐ MAJOR	☐ ≥ 1 minor from skin, CVS, GI or elevated MCT
Level 3		☐ Minor		☐ ≥ 1 minor criterion from at least 2 different systems: ☐ Skin ☐CV ☐GI ☐Elevated MCT
			☐ Minor	☐ ≥ 1 minor criterion from at least 2 different systems: ☐ Skin ☐CV ☐GI ☐Elevated MCT
Level 4	Reported anaphylaxis with insufficient evidence to meet any of levels of diagnostic certainty			
Level 5	**Not a case of anaphylaxis:** if onset not sudden and did not progress rapidly			

Adrenaline Time	Adrenaline Dose	Transfer to ED (Name)	Transfer Time

MCT= Mast Cell Tryptase; For Level 2, a Skin MAJOR can count as a minor criterion

LOGIC TO DETERMINE LEVEL OF DIAGNOSTIC CERTAINTY

Level of Certainty	Logic to reach level of certainty for Anaphylaxis
Level 1, 2 & 3	**Must meet both of the following criteria (if one or both not met, it is not a case – level 5):** ___Sudden onset of symptoms/signs ___Rapid progression of symptoms/signs
Use the pattern of MAJOR and minor criteria met for skin, respiratory, cardiac and gastrointestinal (GI) systems and laboratory result from the table above to determine the highest level of diagnostic certainty (with level 1 > level 2 > level 3).	
Level 1	≥1 Skin MAJOR AND [≥ 1 Respiratory MAJOR AND / OR ≥ 1 Cardiac MAJOR]
Level 2 *NOTE: 4 different ways to meet level 2*	1. ≥ 1 Skin MAJOR AND [≥ 1 Respiratory minor AND / OR ≥ 1 Cardiac minor]
	2. ≥ 1 Respiratory MAJOR AND ≥ 1 Cardiac MAJOR
	3. ≥ 1 Respiratory MAJOR AND ≥ 1 minor from a different system (Skin, Cardiac, GI, lab)
	4. ≥ 1 Cardiac MAJOR AND ≥ 1 minor from a different system (Skin, Respiratory, GI, lab)
Level 3 *NOTE: 2 different ways to meet level 3*	1. ≥ 1 Respiratory minor AND ≥ 1 minor from each of 2 different systems (Skin, Cardiac, GI, lab)
	2. ≥ 1 Cardiac minor AND ≥ 1 minor from each of 2 different system (Skin, Respiratory, GI, lab)
Level 4	Reported anaphylaxis with insufficient evidence to meet any of levels of diagnostic certainty
Level 5	**Not a case of anaphylaxis:** if unable to check 1.1 and 1.2 (i.e., onset not sudden and did not progress rapidly)

Memo

COVID-19 Vaccine Independent Safety Monitoring Board update

Date:	08 July 2021
To:	COVID-19 Vaccine and Immunisation Programme Steering Group
Copy to:	Jo Gibbs, National Director - COVID-19 Vaccine & Immunisation Programme; Dr Ian Town, Chief Science Advisor, Dr Tim Hanlon, Group Manager Post Event/Workstream Lead - COVID-19 Vaccine & Immunisation Programme
From:	Mr John Tait, Chair – COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Information

Purpose of report

1. This memo is to provide an update on the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) and their work to date.

Background and context

2. The CV-ISMB is established to provide expert advice around the safety of COVID-19 vaccines to the Centre for Adverse Reactions Monitoring (CARM), Medsafe, the COVID-19 Vaccine and Immunisation Programme (CVIP) and the Ministry of Health.
3. The Board has expertise from clinical medicine (including neurology, clinical pharmacology and paediatrics), general practice, microbiology and biostatistics. The Board includes members who represent the voice of Māori and Pasifika, along with a lay person to represent the interests of the consumer.
4. The Board meets monthly to discuss cases of note (i.e., adverse events of special interest), with updates from Medsafe on safety data including signals under investigation. There is also provision for ad hoc meetings where the Board can be brought together to discuss an urgent issue.

Key updates & information

5. The CV-ISMB has had five regular working meetings to date (last meeting 24 June) and an ad hoc meeting (22 April) which was called by Medsafe to look at the blood clotting/bleeding effects reported in some of the COVID-19 vaccines being used overseas.

6. Generally, the reported adverse events following immunisation (AEFI) for the Pfizer-BioNTech vaccine in New Zealand, align with what we would expect from the product label and what has been observed to date internationally. Of the reported AEFI to date, ~4% have been classified as serious, with most of these being allergic type reactions (e.g. angioedema, throat tightness and a small number of anaphylaxis cases). Most reports are being submitted to CARM and are mainly for expected reactions (e.g. fever, headache, myalgia and fatigue).

Potential signals under investigation

7. Medsafe present the CV-ISMB detailed analysis of potential safety signals under investigation, with the CV-ISMB providing feedback around actions to take in the New Zealand context (e.g., continue normal pharmacovigilance monitoring, issue a monitoring communication or an update to the product label). Where needed additional expertise is drawn on from outside the Board (e.g., both a haematologist and cardiologist have been engaged).

8. The potential safety signals for the COVID-19 vaccines presented and discussed by the CV-ISMB to date are thrombosis with thrombocytopenia syndrome (TTS) for the Janssen vaccine. Myocarditis, appendicitis, herpes zoster, stroke, menstrual irregularities and pancreatitis for the Pfizer-BioNTech vaccine.

9. Following advice from the CV-ISMB, Medsafe issued Monitoring Communications for TTS and myocarditis (Appendix 1). At the current time with the available evidence, the CV-ISMB agreed that Medsafe should continue to monitor appendicitis, herpes zoster, menstrual irregularities and pancreatitis through normal pharmacovigilance activities.

Myocarditis

10. Myocarditis is an adverse event of special interest for the COVID-19 vaccines and is being monitored closely by CARM, Medsafe and the CVIP. An M^2 monitoring communication was issued by Medsafe on the 9th June; this is where Medsafe is actively seeking further reports of any events of this nature.

11. Medsafe first presented an update on myocarditis to CV-ISMB on 27th May, with a further update provided at the most recent meeting (24 June). Up to the 7th July, CARM had received 10 reports of myocarditis and/or pericarditis for the COVID-19 vaccine. s 9(2)(a) [redacted]

Pancreatitis

12. At the last meeting (24 June), Medsafe presented a case of s 9(2)(a) [redacted] The CV-ISMB agreed that there will be some rare events that happen which we might not fully understand and advised Medsafe to continue monitoring through normal pharmacovigilance.

Reported Deaths

13. All reports of death for the COVID-19 vaccine received by CARM up until the 24th June have been presented to the CV-ISMB; with a number of these deaths being in frail elderly. The CV-ISMB commented that there is a need to be careful attributing death to natural causes in the frail elderly, as they can pass away from mild external stress, such as vaccination.
14. The CV-ISMB expressed concern about vaccinating elderly people with a limited life expectancy and were pleased that this was due to be considered by the COVID-19 Vaccine Technical Advisory Group.

Hypersensitivity/Anaphylaxis reactions

15. The CV-ISMB previously agreed on the 11th March 2021, that potential anaphylaxis reports should be assessed against the Brighton Collaboration case definition for anaphylaxis to determine whether a reaction constitutes anaphylaxis.
16. The rate of reported anaphylaxis (Brighton Level 1-3) in New Zealand is ~18 cases per million doses (24 June) for the CVIP while the reported rate for the Pfizer-BioNTech vaccine in general is ~3-11 cases per million. The CV-ISMB is reassured by the current rate and commented that it is similar to the Centers for Disease Control and Prevention (CDC) and that New Zealand is likely to see higher rates as there is a robust reporting system.
17. The CV-ISMB is pleased to see the Brighton criteria for anaphylaxis being applied in the medical assessment of these reports; with the collection of data to be further strengthened with implementation of the anaphylaxis checklist at the vaccination site.

General

18. It is hoped to bring the CV-ISMB together for a face to face working meeting in August as the CVIP roll out continues into group 4; details and planning for this is currently being worked through.

Recommendations

It is recommended that you:

1.	note	The update of the COVID-19 Vaccine Independent Safety Monitoring Board provided in this Memo	Yes/No

Appendix 1

Thrombosis with Thrombocytopenia Syndrome Monitoring Communication [link]

Safety Information

Published: 27 April 2021

Monitoring Communication

COVID-19 vaccines and rare cases of blood clots with bleeding: no current risk with Comirnaty (Pfizer/ BioNTech) vaccine

27 April 2021

Medsafe has completed a review of the risk of rare cases of blood clots with bleeding (Thrombosis with Thrombocytopenia Syndrome; TTS), reported internationally with some COVID-19 vaccines. At the current time, there is no evidence of a risk of TTS with the Comirnarty (Pfizer/ BioNTech) vaccine.

Additional infomation
Regulator actions
Reporting

Additional information

Medsafe has finished an initial evaluation of international reports of a rare syndrome of blood clots (thrombosis) occurring with bleeding (due to thrombocytopenia) and platelet factor 4 antibodies. To date, all the cases that have been reported after vaccination are linked to the first dose of Vaxzevria (AstraZeneca) or the Janssen COVID-19 vaccines. These vaccines are not currently used in New Zealand.

There have been reports of blood clots internationally after vaccination with Comirnaty. Medsafe's assessment is that there is no indication that these cases are in any way similar to the TTS cases reported with the other COVID-19 vaccines. This assessment was endorsed by New Zealand's COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) on 22 April 2021.

Up to 22 April 2021, the Centre for Adverse Reaction Monitoring (CARM) has received three cases of thrombosis (one stroke, one deep vein thrombosis and one cerebral venous sinus thrombosis). There was no evidence of bleeding in any of these cases. Following review by CARM and the CV-ISMB, none of these cases was considered to be related to vaccination. The number of cases of thrombosis reported following vaccination is lower than the expected number occurring without vaccination. There are over 3,000 cases of thromboembolism and more than 10,000 cases of stroke requiring hospital treatment per year in New Zealand.

Search for consumer medicine information and data sheets

Regulator actions

Medsafe continues to monitor this safety signal and remains in contact with international regulators.

Reporting

Consumers and healthcare professionals are encouraged to report suspected adverse events following immunisation to the Centre for Adverse Reactions Monitoring (CARM).

MINISTRY OF HEALTH
MANATŪ HAUORA

Myocarditis Monitoring Communication [link]

Safety Information

Published: 9 June 2021

Monitoring

Patients should **NOT** decline vaccination subject to a monitoring communication. If you have any concerns with your vaccination, please contact your healthcare professional. A monitoring communication does not mean that the vaccine, medicine or medical device causes an adverse reaction.

Myocarditis – a potential adverse reaction to Comirnaty (Pfizer COVID-19 vaccine)

Description
Monitoring finishes on 31 December 2021

Medsafe is investigating a potential risk of myocarditis following vaccination with Comirnaty. The aim of this communication is to encourage further reports to obtain more information on this potential safety concern.

Medsafe has received two reports of myocarditis (inflammation of the heart muscle) and two reports of myo pericarditis (inflammation of the bag like membrane around the heart as well as the heart muscle) following vaccination with Comirnaty. A small number of myocarditis cases have also been reported in some other countries, such as Israel and the United States. The myocarditis in these cases has generally been mild and not required treatment. There is currently no suggestion that these cases are due to the vaccine but Medsafe is collaborating with international medicine regulators on this issue.

Products affected
Additional information
Regulator actions
Reporting

Products affected

Product name	Sponsor
Comirnaty	Pfizer BioNTech

Additional information

Comirnaty is an mRNA vaccine given to prevent coronavirus disease 2019 (COVID-19) in adults and adolescents who are 16 years of age and older.

Myocarditis is an inflammation of the heart muscle wall. There are many possible causes of myocarditis, the most common being viral infection. Over 100 people are discharged from hospital with a principle diagnosis of myocarditis in New Zealand every year. Symptoms may be non specific, such as constant tiredness and weakness or cough, or specific to the heart, such as chest pain or palpitations (a sensation of rapid or irregular heartbeat).

Most reported cases of myocarditis after vaccination with Comirnaty appear to be mild and occur within a week after receiving the vaccine, and the person has recovered without treatment. Predominantly adolescents and young adults have been affected and more commonly males. No causal association with the vaccine has been concluded.

The benefits of the Comirnaty vaccine still outweigh the risks.

Information about Comirnaty, including known side effects, can be found in the consumer medicine information (CMI) and data sheet.

Regulator actions

This issue was discussed with Medsafe's Independent Safety Monitoring Board (ISMB) on 27 May. The recommendation from ISMB was to highlight this potential adverse reaction to Comirnaty as a Monitoring Communication.

Reporting

Please report any case of myocarditis in patients who have been vaccinated with Comirnaty. Please include information on:

- the time between vaccination and onset of myocarditis
- if any treatment was required
- if any other medicines are being taken
- any relevant medical history
- if it occurred after the first or second dose of Comirnaty

Consumers and healthcare professionals are encouraged to report suspected adverse reactions to medicines to the Centre for Adverse Reactions Monitoring (CARM).

Memo

COVID-19 Vaccine Independent Safety Monitoring Board meeting 9th August 2021 – reported death of concern

Date:	12 August 2021
To:	Dr Ashley Bloomfield, Director-General of Health; Jo Gibbs, National Director - COVID-19 Vaccine & Immunisation Programme
From:	Mr John Tait, Chair – COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Action

Purpose of report

1. This memo seeks to provide an overview of the COVID-19 Vaccine Independent Safety Monitoring Board's (CV-ISMB) meeting held on Monday 9 August 2021 to discuss a fatal report of concern in an individual following COVID-19 vaccination.
2. Following the meeting the Board has prepared a statement outlining their findings.

Background and context

3. On 2 August 2021, the Centre for Adverse Reactions Monitoring (CARM) received a report from a forensic pathologist of an individual who had passed away ~4 days after their first dose of the Pfizer/BioNTech vaccine. Myocarditis was a finding of the post-mortem that had not been recognised prior.
4. Follow up investigation with the forensic pathologist, s 9(2)(a) and the general practitioner of the individual indicated that the myocarditis could potentially be temporally linked to the individual's first vaccination event.
5. Based on this information Medsafe and the COVID-19 Vaccine & Immunisation Programme (CVIP) requested an extraordinary meeting of the CV-ISMB to discuss the details of this case in order to assess an association with the Pfizer/BioNTech vaccine.
6. The CV-ISMB was convened for a meeting on 9 August 2021 where an overview of the case was provided by Dr Michael Tatley, Director of CARM, followed by a presentation from the forensic pathologist, s 9(2)(a) The Board was also in receipt of expert opinion from cardiologist, Professor Ralph Stewart who has recently been appointed to the Board.
7. Dr s 9(2)(a) has sent histology slides to cardiac pathologists in the United Kingdom and United States for review to confirm the myocarditis type.

Statement from the Board

The COVID-19 Vaccine & Immunisation Programme has recently been informed of the death of a s 9(2)(a) a few days after s 9(2)(a) received s 9(2)(a) first dose of the Pfizer/BioNTech vaccine.

We extend our sympathies to the family, whānau and friends of this individual.

This death has been reported to the Coroner who is investigating. A post-mortem has been performed which identified the initial cause of death as myocarditis.

Due to the seriousness of this case, the COVID-19 Vaccine Independent Safety Monitoring Board met on August 9th to discuss the details of the case in relation to a possible link to vaccination.

The Board has considered the potential causes of the individual's myocarditis, including the Pfizer/BioNTech vaccine. The Board noted that:

- The Pfizer/BioNTech vaccine and some other COVID-19 vaccines increase the risk of myocarditis; Medsafe issued an Alert communication for myocarditis caused by the Pfizer/BioNTech vaccine on 21 July 2021.
- COVID-19 infection increases the risk of myocarditis substantially more than COVID-19 vaccination.
- There are many possible causes of myocarditis, the most common being viral infection; over 100 people are discharged from hospital with a principle diagnosis of myocarditis in New Zealand every year.
- In this case other factors which may have potentially caused the myocarditis or led to a more severe myocarditis have been identified.
- The individual had no symptoms prior to the vaccine and the symptoms of myocarditis developed in the days immediately following s 9(2)(a) first vaccine dose.

It is the opinion of the Board, with the current available information, that the vaccination event was the likely cause of the myocarditis.

The Board considers that the circumstances of this case do not impact or change the known information on myocarditis, and the benefits of vaccination with the Pfizer/BioNTech vaccine for COVID-19 continue to greatly outweigh any risk of such rare side effects. The Pfizer/BioNTech vaccine data sheet and consumer medicine information were recently updated based on international evidence to include information about myocarditis as a rare side effect.

The Board noted COVID-19 infection can itself be a cause of myocarditis as well as other serious illnesses and it remains safer to be vaccinated than to be infected with the virus.

The Board wishes to remind healthcare professionals and consumers to be alert to the symptoms of myocarditis that may include new onset chest pain, shortness of breath or abnormal heartbeat.

8. The minutes for the meeting have been attached for your reference (Appendix 1).

Recommendations

It is recommended that you:

1.	note	Contents of this memo	Yes/No
2.	agree	For the COVID-19 Vaccine & Immunisation Programme to action communications on awareness of myocarditis	Yes/No

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

Signature _____ Date:
Jo Gibbs
National Director CVIP

Document 4

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

COVID-19 Vaccine Independent Safety Monitoring Board – reported death of concern

Date:	17 September 2021
To:	Dr Ashley Bloomfield, Director-General of Health; Jo Gibbs, National Director - COVID-19 Vaccine & Immunisation Programme
From:	Mr John Tait, Chair – COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Action

Purpose of report

1. This memo seeks to provide an overview of the COVID-19 Vaccine Independent Safety Monitoring Board's (CV-ISMB) review of the reported death of a teenager following their first dose of the Pfizer/BioNTech vaccine.
2. Following the meeting the Board has prepared a statement outlining their findings.

Background and context

3. On Monday 13th September the Centre for Adverse Reactions Monitoring (CARM) received a report from a relative of an individual who had passed away ~12 days after their first dose of the Pfizer/BioNTech vaccine.
4. This case had also been reported in the media and across social media in the preceding weekend.
5. Follow up investigation indicated a report for this individual had also been submitted to CARM through their traditional channels, with the combined oral contraceptive considered the suspect medication.
6. Due to concern from the public and the level of information being spread across social media, Medsafe and the COVID-19 Vaccine & Immunisation Programme (CVIP) requested that this case be included on the agenda for the regular CV-ISMB meeting scheduled for Wednesday 15th September.
7. At the meeting, Dr Michael Tatley, Director of CARM, provided the Board with an overview of the case, with information obtained from the attending emergency department physician and forensic pathologist. The Board was also in receipt of expert opinion from haematologist, Dr Laura Young, who specialises in clotting disorders, recently appointed to the Board.
8. s 9(2)(a) [redacted]

9. It was noted by the Board that it would be helpful for a thrombophilia screen to be completed along with follow up information from the individual's General Practitioner around the specific COC prescribed, indication and when this was started; however this would not change the view of the Board.

Statement from the Board

The Ministry of Health COVID-19 Vaccine & Immunisation Programme (CVIP) has recently been informed of the death of a s 9(2)(a) [redacted], which occurred 12 days after s 9(2)(a) [redacted] first dose of the Pfizer/BioNTech vaccine (Comirnaty).

We extend our sympathies to the family, whānau and friends of this individual.

This death has been reported to the Coroner who is investigating. A preliminary post-mortem has been performed which identified the cause of death as pulmonary thromboembolism.

The COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB), referred hereto after as 'the Board', met on 15th September where details of the case were considered with a view to examining whether there was a possible link to vaccination.

The Board has considered the potential causes of the individual's pulmonary embolism, including the Pfizer/BioNTech vaccine. The Board noted that:

- s 9(2)(a) [redacted]
- Venous thromboembolism (deep vein thrombosis and pulmonary embolism) is a rare side effect of s 9(2)(a) [redacted] use. Cases of venous thromboembolism most frequently occur in the first 12 months of s 9(2)(a) [redacted] use.
- There have been fatal reports for venous thromboembolism to the Centre for Adverse Reactions Monitoring (CARM) associated with the s 9(2)(a) [redacted] in the past.
- The individual had symptoms (including breathlessness) prior to vaccination.
- Thrombosis events have been reported as occurring in temporality with the Pfizer/BioNTech vaccine, but large studies have found no increase risk compared to matched controls not vaccinated.
- Venous thrombosis events occur regularly in the general population, including in young people and can be attributed to a variety of factors.

It is the opinion of the Board, with the current available information, that the pulmonary embolism was unlikely to be related to the administration of the Pfizer/BioNTech vaccine in this individual.

The Board noted that expert haematology advice has been sought regarding other factors potentially involved.

The Board did not consider it within its remit to investigate the relationship of this death to s 9(2)(a) [redacted] use. The Centre for Adverse Reactions Monitoring (CARM) has been notified of this association and CARM reports such matters to the Medicines Adverse Reactions Committee.

The Board considers that the circumstances of this case do not impact or change the known information on the side effect profile of the Pfizer/BioNTech vaccine, and the benefits of vaccination continue to greatly outweigh the risks of adverse effects.

Recommendations

It is recommended that you:

1.	note	Contents of this memo	Yes/No

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

Signature _____ Date:
Jo Gibbs
National Director CVIP

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

COVID-19 Vaccine Independent Safety Monitoring Board – underreporting in certain populations and communication around post-mortems

Date:	04 October 2021
To:	Jo Gibbs, National Director, COVID-19 Vaccine & Immunisation Programme
Copy to:	Chris James, Group Manager, Medsafe; Dr Tim Hanlon, Group Manager Post Event, COVID-19 Vaccine & Immunisation Programme
From:	Mr John Tait, Chair, COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Decision

Purpose of report

1. This memo seeks to provide an overview of the COVID-19 Vaccine Independent Safety Monitoring Board's (CV-ISMB) discussion and recommendations on:
    i. underreporting in certain populations
    ii. communication around post-mortems

Background and context

2. The CV-ISMB met on Wednesday 15 September, where an overview of the reported adverse events following immunisation (AEFI) for the Pfizer/BioNTech vaccine in New Zealand was provided by Medsafe.
3. At this time there were 17,182 reported AEFI of which 688 had been classified as serious. Detail was provided to the Board about the number of reports by system organ class, ethnic group and age group at vaccination date.
4. A particular focus was given to reports by ethnic group with analysis of the common symptoms and reporter type.
5. From the information presented, it was clear to the Board that there is underreporting for Pacific Peoples with a reporting rate of 0.25%, while the reporting rates for Māori 0.34% and Asian 0.3% were also lower than overall reporting rate (Appendix 1).
6. Although there was no clear difference in the symptoms reported from the available data, it was evident that there is a lack of engagement with consumer reporting for Pacific Peoples (Appendix 2).
7. It was noted that Pacific Peoples do under report; the main concern is that although AEFI are happening, if reported this will generally be delayed (e.g., come up in passing during a consultation). It was also highlighted that there is uncertainty around what should be reported, and language barriers could be also creating an obstacle to reporting.

8. The Board proposed that a communication could be made to the public that Pacific Peoples are not actively reporting on AEFI and simple guidance provided to the public may help this. It was felt that consideration should also be given to translation of any communication, to enable better access.

9. The Board considered that if reporting was emphasised for Pacific Peoples, that this would likely have a positive impact on reporting rates for all groups.

10. In addition to the issue of underreporting the Board also considered a number of fatal reports. The Board noted that, access to the post-mortem report and confidence that all the necessary evaluations had been conducted would allow a more robust and timely assessment around if there was a link to the vaccination event.

11. It was also noted by the Director of the Centre for Adverse Reactions Monitoring (CARM) that he had been contacted by a couple of pathologists seeking advice on the type of tests and investigations that would be useful for the investigation of the role of vaccination in fatal cases.

12. The Board considered it would be beneficial to the investigation of these cases if a couple of communications were made to the Sector:

    i. to encourage intensive care clinicians and cardiologists to consider post-mortems where the cause of death was unclear and there had been a recent vaccination

    ii. to pathologists, in cases of sudden cardiac death a cardio histology should ideally be conducted where there had been a recent vaccination event to discount the cause of death as due to myocarditis.

13. Following the meeting on the 15 September of the Board, both these issues were further discussed at a in person meeting last week with the Director of CARM, Group Manager Post Event and Manager, Clinical Risk Management, Medsafe where a memo was agreed.

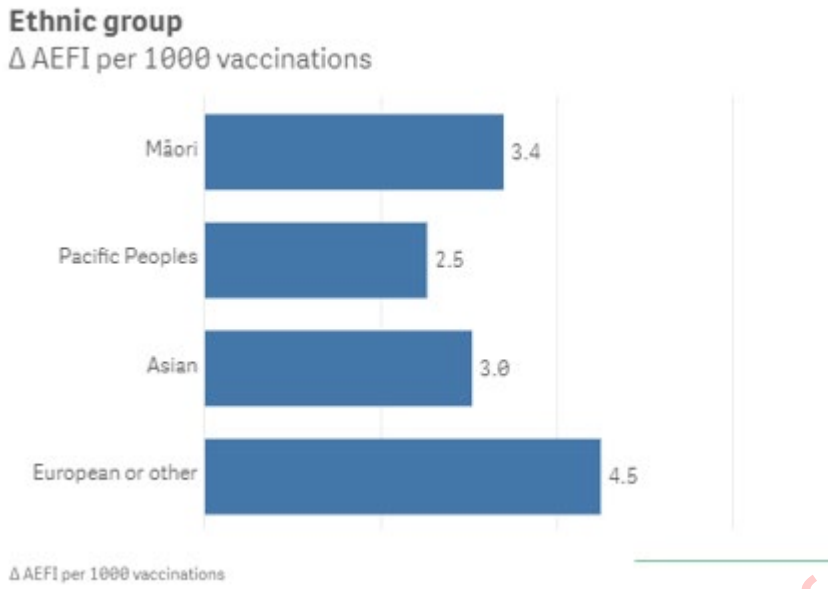
Recommendations

It is recommended that you:

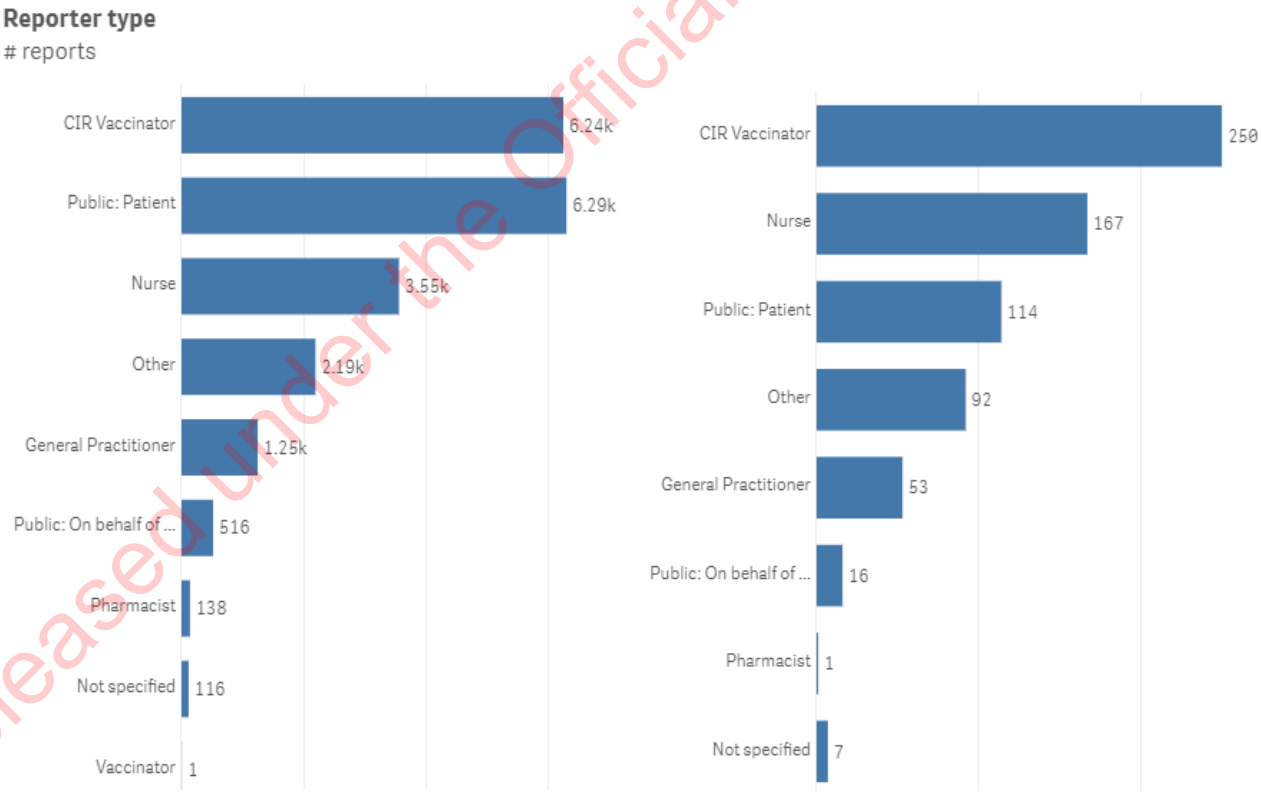
1.	note	The contents of this memo	Yes/No
2.	agree	For the COVID-19 Vaccine & Immunisation Programme to action communications around underreporting of AEFI in Pacific Peoples.	Yes/No
3.	agree	For a communication to be prepared by the CV-ISMB and distributed by the Programme around consideration of post-mortems where the cause of death is unclear and there has been a recent vaccination event.	Yes/No
4	agree	For a communication to be prepared by the CV-ISMB and sent by the Programme to pathologists encouraging a cardio histology be conducted in cases of sudden cardiac death in individuals following vaccination.	Yes/No

Signature _____ Date:
Jo Gibbs
National Director
COVID-19 Vaccine and Immunisation Programme

Appendix 1 – Reporting rate by ethnic group (14 September)



Appendix 2 – Reporter type (14 September)



Overall reporter type

Pacific Peoples reporter type

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) tenure

Date:	11 October 2021
To:	Dr Ashley Bloomfield, Director-General of Health; Jo Gibbs, National Director, COVID-19 Vaccine & Immunisation Programme
Copy to:	Chris James, Group Manager, Medsafe; Dr Tim Hanlon, Group Manager Post Event, COVID-19 Vaccine & Immunisation Programme
From:	Mr John Tait, Chair, COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Decision

Purpose of report

1. This memo seeks to provide an overview of the considerations for the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) as the COVID-19 Vaccine and Immunisation Programme (CVIP) transitions to a future state.

Background and context

2. The CV-ISMB is an independent panel of experts from clinical medicine, microbiology and biostatistics, established to support the review of safety information for the COVID-19 vaccines. The Board provides recommendations and advice to the Centre for Adverse Reactions Monitoring, Medsafe, the CVIP and Ministry of Health.
3. The Board held their first meeting on the 25th February 2021 and currently meets every three-four weeks to discuss and review potential safety signals, adverse events of special interest and other reports of note; there is also the provision for the Board to hold 'extraordinary' meetings to discuss a serious unexpected event or issue of concern with urgency.
4. The current membership of the Board stands at 15 (refer Appendix 1) with key specialities including neurology, cardiology, haematology and paediatrics included, along with representation for both Māori and Pasifika. The Board also holds a position for a lay person (non-healthcare professional) to represent consumer interests.
5. Members of the Board are engaged with meetings and these are attended by most of the group, with active engagement and feedback provided in discussions and recommendations made to CARM, Medsafe and the CVIP.
6. In a meeting held on 29 October, with the Director of CARM, Group Manager Post Event, CVIP and Manager, Clinical Risk Management, Medsafe the scheduled end of the CVIP was discussed, along with what a future state might look like as vaccinations continue into 2022 and a possible National Immunisation Unit is established.

7. It was evident from these discussions that the role of the CV-ISMB is still needed to support the safety surveillance of the COVID-19 vaccines for the foreseeable future; an interim report for the Board (February-October) is currently being prepared, however key areas of need for the Board in the short-medium term are outlined below.

CV-ISMB work for November and beyond

8. Rapid cycle analysis work setup within the CVIP for real time observed versus expected analysis of adverse events of special interest (including deaths) is supported by a working group made up of members of the CV-ISMB for refinement of the criteria used. The results of these analyses are discussed and validated with the Board. Some of this work has recently shared been shared as part of the recent Medsafe Weekly Safety Report (#28) and could become a key tool to help instil confidence in the safety of the vaccine.

9. The pending introduction of new vaccine (s) to the New Zealand schedule for COVID-19, will have implications for safety surveillance, especially considering both the Janssen and AstraZeneca vaccines are known to cause thrombosis with thrombocytopenia syndrome (TTS) in certain populations. The potential use of booster doses will also require careful monitoring and messaging around safety, to help support uptake if the eligible population is required to have a third dose.

10. Myocarditis has been found to be an unexpected side effect with the Pfizer/BioNTech vaccine. As part of the work around the monitoring of this adverse event of special interest, the need for a deep dive follow-up of reported cases of myo-/peri/myoperi-carditis has been established. This will require longitudinal follow-up to determine what the nature of these reactions has been. This work will be undertaken in conjunction with Medsafe and will, ideally, be publishable.

11. The Board will have a key role in cases such as vaccination in pregnancy and follow up postpartum for congenital abnormalities. This data will start to be available in early 2022 when pregnancies are completed and will be ongoing work undertaken in conjunction with Medsafe.

12. In addition, there will be a need to consider the role of a future Independent Safety Monitoring Board and whether the current CV-ISMB transitions into a National Immunisation Technical Advisory Group (NITAG) beyond the COVID-19 vaccine rollout and into the possible National Immunisation Unit or whether this function is absorbed into the work of the Medicines Adverse Reactions Committee (MARC).

Recommendations

It is recommended that you:

1.	note	The contents of this memo	Yes/No
2.	agree	The CV-ISMB will continue its tenure for at least the first quarter of 2022 with the determinate for the future after that.	Yes/No
3.	agree	That adequate secretariat support will be available to the CV-ISMB for the rest of 2021 and the first quarter of 2022.	Yes/No

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

Signature _____ Date:
Jo Gibbs
National Director
COVID-19 Vaccine & Immunisation Programme

Appendix 1: CV-ISMB membership

Name	Area of Expertise	Position
Mr John Tait (Chair)	Obstetrics	Chief Medical Officer CCDHB; Consultant obstetrician and gynaecologist
Honorary Associate Professor Hilary Longhurst (Deputy Chair)	Immunology; Pathology	Senior Medical Officer, Immunology
Dr Nick Cutfield	Neurology	Consultant Neurologist and Clinical Lead; Senior Lecturer
Associate Professor Matt Doogue	Clinical Pharmacology; Endocrinology	Consultant physician in Clinical Pharmacology and General Medicine
Dr Kyle Eggleton	General Practice	Kaupapa Māori Medical Officer at Ki A Ora Ngātiwai; Senior Lecturer
Professor Chris Frampton	Biostatistics	Professor of Biostatistics
Dr Maryann Heather	General Practice; Pacific Health	GP at South Seas Healthcare; Senior Lecturer
Dr Tom Hills	Immunology	Chief Medical Resident, Immunology
Professor Thomas Lumley	Biostatistics	Professor of Biostatistics
Saskia Schuitemaker	Lay person – to represent consumer interests	Coordinator, Child and Youth Mortality review Group, Waikato District Health Board
Dr Owen Sinclair, Te Rarawa	Paediatrics, Māori Health	Paediatrician WDHB
Professor Lisa Stamp	Rheumatology	Professor in Medicine; Rheumatologist
Dr Anja Werno	Microbiology; Pathology	Chief of Pathology & Laboratories, Acting Clinical Director of Microbiology, CHL; Clinical Senior Lecturer, University of Otago
Dr Enver Yousuf	General Medicine	Senior Registrar CCDHB General Medicine
Professor Ralph Stewart	Cardiology	Clinical Professor of Medicine; Cardiologist
Dr Laura Young	Haematology	Haematologist Clinical Lead (Specialising in clotting disorders)

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

COVID-19 Vaccine Independent Safety Monitoring Board meeting 8 December 2021 – reported deaths of concern

Date:	13 December 2021
To:	Dr Ashley Bloomfield, Director-General of Health; Astrid Koornneef, Director National Vaccine and Immunisation Programme
From:	Mr John Tait, Chair – COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Decision

Purpose of report

1. This memo seeks to provide an overview of the COVID-19 Vaccine Independent Safety Monitoring Board's (CV-ISMB) meeting held on Wednesday 8 December 2021 to discuss three fatal reports of concern in individuals following COVID-19 vaccination.
2. Following the meeting, the Board has prepared a statement outlining their findings and provided recommendations for the COVID-19 Vaccine and Immunisation Programme (CVIP).

Background and context

3. In the week commencing 29 November 2021, the Centre for Adverse Reactions Monitoring (CARM) received three fatal reports for individuals who passed away in the period following vaccination where vaccine-mediated myocarditis was proposed as the cause of death.
4. Two of the reported cases are currently under investigation with the Coroner and were reported to CARM by the pathologists. The third case was reported to CARM by the Chief Medical Officer (CMO) from the respective District Health Board (DHB) following a review by their Adverse Reactions Committee.
5. One case s 9(2)(a) has been discussed in the media and two cases s 9(2)(a) are circulating on social media. High level details of the reported cases:
   - s 9(2)(a) : s 9(2)(a) who passed away 12 days after their first dose of the vaccine. s 9(2)(a)
   - s 9(2)(a) s 9(2)(a) who passed away 11 days after their second dose of the vaccine. s 9(2)(a)
   - s 9(2)(a) s 9(2)(a) who passed away 36 days after their second dose of the vaccine. The death of this individual was not considered to be linked to the

vaccine, however, was reported due to the temporality of the vaccination event following a review at the DHB.

6. Based on this information Medsafe requested an extraordinary meeting of the CV-ISMB to discuss the details of these cases to consider an association with the Pfizer/BioNTech vaccine.

7. The CV-ISMB was convened for a meeting on 8 December 2021 where an overview of the cases was provided by Dr Michael Tatley, Director of CARM. The meeting was also attended by pathologist, s 9(2)(a), who presented s 9(2)(a) findings to date in the case of the s 9(2)(a) and forensic pathologist, s 9(2)(a), and s 9(2)(a) registrar, s 9(2)(a), who presented their findings to date in the case of the s 9(2)(a)

8. s 9(2)(a) had sought advice and guidance in respect of her case from s 9(2)(a), who was the forensic pathologist for the previous case of vaccine-mediated myocarditis reported in New Zealand in August. s 9(2)(a) confirmed at the meeting that her findings had been peer reviewed by an expert cardiac pathologist at the University of California, Los Angeles (UCLA).

9. Medsafe have sought information from other regulators regarding reported fatal cases of vaccine-mediated myocarditis following the Pfizer/BioNTech vaccine and had a call with the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) on Friday 9 December 2021 to discuss this further.

10. Medsafe also provided an update to the Board on the reported cases of myo/peri-carditis in New Zealand, including a breakdown of the reports by age band and dose interval.

Statement from the Board

The COVID-19 Vaccine Independent Safety Monitoring Board was informed of three reports of people who had died in the period following vaccination with a potential myocarditis. The Board met to review the available information related to these cases to determine whether the Pfizer (Comirnaty) COVID-19 vaccine was a factor.

The Board extends its deepest sympathies to the family, whānau and friends of the people involved.

Due to the seriousness of these reports, the Board met on 8 December 2021 to discuss the details of these three cases in relation to a possible link to vaccination.

The death a of s 9(2)(a) was discussed at length, however further information is required before a determination on the role of the vaccine can be made. A further statement will be made when that information is available. Two of the cases are considered further below. Having reviewed the information, the Board considers that the myocarditis which was implicated in the death of a s 9(2 s 9(2)(a), was unlikely related to vaccination. The time from vaccination to the onset of symptoms and clinical factors point to other causes and is not consistent with a causal link.

The Board considered in detail the death of a s 9(2)(a), who died within 2 weeks of s 9(2)(a) first dose of the Pfizer vaccine. This case has been reported to the Coroner, who is investigating. Preliminary information from the post-mortem examination has identified myocarditis as the likely cause of death in this individual.

The Board has considered the potential causes of myocarditis in this individual, including the Pfizer vaccine. The Board noted:

- There were no reported symptoms prior to the vaccine and the symptoms of myocarditis developed in the days immediately following s 9(2)(a) first vaccine dose.
- The individual had not sought medical advice or treatment for s 9(2)(a) symptoms.
- Some COVID-19 vaccines, including the Pfizer vaccine increase the risk of myocarditis; Medsafe issued an Alert communication for myocarditis as a rare adverse reaction of the Pfizer vaccine on 21 July 2021.
- COVID-19 infection increases the risk of myocarditis substantially more than vaccination with the Pfizer vaccine.
- There are many possible causes of myocarditis, the most common being viral infection; an average of 95 people (SAFE study) are discharged from hospital with a principle diagnosis of myocarditis in New Zealand every year.
- Myocarditis is a treatable condition, if identified, and outcomes are better the earlier that treatment is started.
- With the current available information, the vaccination event was the probable cause of the myocarditis in this individual.

The Board considers that the circumstances of these cases do not impact or change the known information on myocarditis, and the benefits of vaccination with the Pfizer vaccine for COVID-19 continue to greatly outweigh the risk of such rare side effects. The Board have recommended actions to be taken by the COVID-19 Vaccine and Immunisation Programme to continue to highlight myocarditis as a very rare side effect of the Pfizer vaccine.

The Board noted COVID-19 infection can itself be a cause of myocarditis as well as other serious illnesses and it remains safer to be vaccinated than to be infected with the virus.

The Board wishes to remind healthcare professionals and consumers to be alert to the symptoms of myocarditis that may include chest pain, tightness or discomfort, shortness of breath or abnormal heartbeat (and/or accompanied by fever). The Board highlighted that discussion at the time of vaccination, should include information on common expected side effects and rare side effects, along with when and how to seek medical advice.

11. The Board emphasised the tragic nature of these cases and felt that this provided the opportunity for a review of the information provided to consumers and healthcare professionals around myo/peri-carditis. It was felt that consideration be given to:

    i. Updating outward communications to the public on symptoms of potential myo/per-carditis (e.g., is chest pain sufficient or is this better reflected as chest tightness and/or chest discomfort).

    ii. Ensuring that information on side effects is detailed at the time of vaccination; individuals need to be provided with verbal alongside written information about what to expect after their COVID-19 vaccine. This should include discussion of common and rare side effects and when/where/how an individual can seek medical advice.

    iii. An update to the healthcare sector, in particular vaccinators, Whakarongorau, General Practitioners and Emergency Departments about the risk of myocarditis with the Pfizer/BioNTech vaccine and the signs/symptoms of this.

12. The Board noted that aspiration prior to injection of the Pfizer/BioNTech vaccine does not routinely take place, based on information in the Immunisation Handbook. The Board were informed about a murine study in which mRNA COVID-19 vaccine was administered by either the intra-muscular (IM) or intra-venous (IV) route. In this study, myocarditis was observed in some mice; these mice were all observed to have received the vaccine via the IV route. The COVID-19 Vaccine Technical Advisory Group (CV TAG) have been kindly asked to pick this up.

13. The Board continues to review emerging literature and reports from other jurisdictions and the manufacturers regarding the safety of the COVID-19 vaccines. Recommendations form the Board for the CVIP following this meeting are outlined below.

14. The Board did not raise concerns about the benefit risk balance for the Pfizer/BioNTech COVID-19 vaccine but emphasised that actions should be taken to reduce the risk of harm as emphasised above.

15. The minutes for the meeting have been attached for your reference (Appendix 1). *Minutes were provided to the Director-General and Director National Vaccine and Immunisation Programme however have been removed from the paper submitted to Steering Group.*

Recommendations

It is recommended that you:

1.	note	Contents of this memo	Yes/No
2.	approve	That the statement from the Board will be published on the Ministry of Health website, following appropriate consultation with all relevant parties.	Yes/No
3	agree	Active communications and, if needed, training to ensure both common and rare side effects are talked about with consumers at the time of vaccination, including how/where/when consumers can seek medical advice.	Yes/No
4	agree	Review of all collateral and messaging for the Pfizer/BioNTech for consumers, to ensure the symptoms and information on myocarditis is clear and easy to understand. Consideration needs to be given to symptoms referenced, for example is 'chest pain' sufficient.	Yes/No
5	agree	Re-emphasis on communications around the signs and symptoms of myocarditis to the healthcare sector, in particular to vaccinators, Whakarongorau, General Practitioners and Emergency Departments	Yes/No
6	note	Medsafe is actively engaging with other regulators to understand whether they have received similar reports; however, the Board does not feel that the current cases impact the benefit/risk consideration for the Pfizer/BioNTech vaccine in the New Zealand.	Yes/No

Signature _____ Date:
Astrid Koornneef
Director National Vaccine and Immunisation Programme

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

Memo

COVID-19 Vaccine Independent Safety Monitoring Board Interim Report

Date:	25 February 2022
To:	National Immunisation Programme Steering Group
Copy to:	Astrid Koornneef, Director, National Immunisation Programme; Dr Tim Hanlon, Group Manager Post Event, National Immunisation Programme; Rachel Lorimer, Group Manager, Communications and Engagement, National Immunisation Programme;
From:	Dr John Tait, Chair, COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Decision

Purpose of report

1. This memo is to provide an overview of the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) Interim Report for 2021 (February-December).

Background and context

2. The CV-ISMB was established in February 2021 to provide expert advice around the safety of COVID-19 vaccines to the Centre for Adverse Reactions Monitoring (CARM), Medsafe, the COVID-19 Vaccine and Immunisation Programme (CVIP) and the Ministry of Health.
3. The Board has expertise from clinical medicine (including neurology, clinical pharmacology and paediatrics), general practice, microbiology and biostatistics. The Board includes members who represent the voice of Māori and Pasifika, along with a lay person to represent the interests of the consumer.
4. Meetings are held every three to four weeks to discuss cases of note, with updates from Medsafe on safety data including signals under investigation. There is also provision for extraordinary meetings where the Board can be brought together to discuss an urgent issue.
5. The Board has the requirement in their Terms of Reference to provide a report to Steering Group at their end date, which was initially anticipated to be December 2021. However, a memo to the Director-General in October 2021 extended this to 31 March 2022.

6. It was agreed by the Board at their meeting on 6 October 2021 that an interim report describing the function, processes and evaluations of the CV-ISMB would be beneficial. It was highlighted by Ministry Communications that a report was important to emphasise the findings of the Board.

Interim Report

7. It was agreed that a report for 2021 (February -December) would be appropriate given that during this period, the Pfizer/BioNTech vaccine was the focus of the roll-out in New Zealand in people aged 12 years and older whilst 2022 was expected to see a more diverse roll out with different vaccines, younger age groups and the wider use of booster doses.

8. The data cut-off for this report is 28 November 2021, at which point only the Pfizer/BioNTech vaccine was available in New Zealand. As at the 28 November almost 90% of the eligible population (12 years and older) had received two doses of the Pfizer/BioNTech vaccine and both a third dose for the immunocompromised (primary course) and booster dose had recently been approved.

9. The CV-ISMB held its first meeting on 11 March 2021 with a further 15 meetings throughout 2021 (including three ad-hoc meetings). Eighteen safety signals for the Pfizer/BioNTech vaccine have been considered, which has led to 28 recommendations to either Medsafe or the Programme. To date only one safety signal has been confirmed, with myocarditis and pericarditis identified as very rare adverse reactions of the Pfizer/BioNTech and added to the product label in July.

10. The Board has been reassured by both the international and New Zealand data presented, that the Pfizer/BioNTech vaccine is a very safe vaccine.

11. The full report is attached as Appendix 1 for your perusal.

Next steps

12. There has been increasing interest in the work of the CV-ISMB throughout 2021 from both the healthcare sector and public. There is currently information available on the CV-ISMB on the Ministry website which provides a brief summary of what the Board does and lists the members.

13. For transparency and to provide further confidence in our safety monitoring systems for the COVID-19 vaccines, it is proposed that a brief introduction be provided on the Ministry website and the full report made available for anyone to read.

14. In addition, Communications will pull key messages from the report and ensure that these are included across safety related content available for the COVID-19 vaccines.

Recommendations

It is recommended that you:

1.	note	The contents of this memo	Yes/No
2.	approve	The publication of the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) Interim Report on the Ministry of Health website	Yes/No
3	agree	To consideration being given to a press release around the publication of the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) Interim Report	Yes/No
4	note	That Communications will ensure that key measures from the report are reflected in safety messaging for the COVID-19 vaccines	Yes/No

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

Memo

COVID-19 Vaccine Independent Safety Monitoring Board update

Date:	25 February 2022
To:	National Immunisation Programme Steering Group
Copy to:	Astrid Koornneef, Director, National Immunisation Programme; Dr Ian Town, Chief Science Advisor; Dr Tim Hanlon, Group Manager Post Event, National Immunisation Programme; Chris James, Group Manager, Medsafe
From:	Dr John Tait, Chair, COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Information

Purpose of report

1. This memo is to provide an update on the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) and recent work.

Background and context

2. The CV-ISMB is established to provide expert advice around the safety of COVID-19 vaccines to the Centre for Adverse Reactions Monitoring (CARM), Medsafe, the National Immunisation Programme (NIP) and the Ministry of Health.
3. The Board has expertise from clinical medicine (including neurology, immunology and paediatrics), general practice, microbiology and biostatistics. The Board includes members who represent the voice of Māori and Pasifika, along with a lay person to represent the interests of the consumer.
4. Meetings are held every three to four weeks to discuss cases of note with updates from Medsafe on safety data including signals under investigation. There is also provision for extraordinary meetings where the Board can be brought together to discuss an urgent issue.

Key updates & information

General

5. When the Board was established in early 2021, 14 members were appointed with the expertise recommended by the World Health Organization for such oversight committees. Two further members were appointed in August 2021, with expertise in cardiology and haematology (specifically clotting

disorders). With the focus now for the COVID-19 vaccines shifting to the vaccination of children, a second paediatrician, Dr Wendy Hunter, was appointed to the Board in February 2022.

6. The CV-ISMB has had two regular working meetings to date in 2022 (26 January and 9 February) and is scheduled to meet again on 2 March to further consider two reported deaths:

   - A s 9(2)(a) who died from a potential vaccine-mediated myocarditis 11 days after their second dose of the vaccine. This case was considered by the Board at an extraordinary meeting held on 8 December, however further information was needed before the Board could make a determination around the role of the vaccine.
   - A s 9(2)(a) who died approximately 8 days after their booster dose of the vaccine. The General Practitioner (GP) for this case had indicated that the vaccine response (fever and nausea) could have been contributory. This case was considered by the Board on 9 February; however, a decision was not reached and further follow up information from the GP/rest home was subsequently sought.

Signals and memos

7. The potential safety signals for the COVID-19 vaccines presented and discussed to date by the CV-ISMB in 2022 are myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and Guillain-Barré syndrome with the Pfizer/BioNTech vaccine.

8. At the current time with the available evidence, the CV-ISMB agreed that Medsafe should continue to monitor myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and Guillain-Barré syndrome through normal pharmacovigilance activities.

9. The CV-ISMB has also been presented memos on the safety information for the AstraZeneca COVID-19 vaccine, 5–11-year-olds and booster doses (Pfizer/BioNTech and AstraZeneca).

AstraZeneca COVID-19 vaccine

10. An update on the AstraZeneca COVID-19 vaccine was provided to the Board on 26 January. At the time of data cut-off (12 January) there had been 170 case reports of adverse events following immunisation (AEFI), with eight of these reports classified as serious (mainly allergic type reactions). Most reports were in people receiving their first dose of a COVID-19 vaccine.

11. The Board felt reassured by the data and commented that Medsafe should continue to closely monitor the AstraZeneca COVID-19 as the reporting in New Zealand might be different to overseas due to how the vaccine is being utilised (i.e., as an alternative for people who have potentially experienced a serious adverse event after a dose of the Pfizer vaccine).

5–11-year-olds

12. An overview of the safety data in 5–11-year-olds was discussed with the Board on 9 February. At data cut-off (30 January) there had been 352 case reports of AEFIs. One report concerned a child admitted to hospital for investigation and monitoring of chest pain was classified as serious. In this case the investigations were reported as normal and there was no evidence of myocarditis or pericarditis.

13. The Board were reassured with the data and agreed with Medsafe's recommendation to continue to monitor the safety of the paediatric Pfizer/BioNTech vaccine closely through routine

pharmacovigilance. Regular updates will be provided to the Board in their scheduled meetings on this data as more of the eligible population is vaccinated and children start receiving their second doses.

14. Two significant concerns were raised by the Board around the roll out of the COVID-19 vaccines in the 5–11-year-olds:

    - One member voiced concern around the inequitable roll out and that this would have safety implications in vulnerable populations.
    - It was also highlighted that an unintended and unfortunate effect of the assiduous focus on the COVID-19 vaccine roll out, is that other immunisation rates are falling substantially, particularly for Māori and Pasifika children. This has serious equity implications, along with there being a high risk of an epidemic.

Boosters

15. The CV-ISMB were also provided an update on the safety data in New Zealand for boosters on 9 February. The Pfizer/BioNTech is currently the only COVID-19 vaccine approved for use by Medsafe (interval of 6 months) and the booster predominantly being used in NZ. There have been a small number of doses of the AstraZeneca COVID-19 vaccine administered as a booster (~600 at data cut-off).

16. Although the safety data is still maturing for the Pfizer/BioNTech vaccine, all adverse events are being reported at a lower rate than for dose one and two, with the exception of lymphadenopathy. It was noted that Pfizer has confirmed there is an increased rate of this adverse event with the booster dose. The Board felt reassured with the information presented and agreed with Medsafe's recommendation to continue to monitor the safety of boosters through routine pharmacovigilance.

Extraordinary meetings

17. The CV-ISMB has held three extraordinary meetings in 2021. Following the extraordinary meeting on 8 December where two of the cases considered were also under coronial investigation, the Chair met with Acting Chief Coroner Tutton to discuss the role of the CV-ISMB in considering deaths potentially linked to the COVID-19 vaccines.

18. An agreement was reached around:

    - The Board being able to request written information from the pathologist prior to a meeting, provided this information is also sent in parallel to the Coroner. It was acknowledged that as this was additional work for the pathologists this may require some formal updating to the contract for these services and potentially a payment mechanism. There is work underway to progress this request.
    - Streamlining the review process by the Coroner for any press releases by the CV-ISMB where a case is under coronial investigation.

19. Additionally, it has become apparent that there is a need for the Ministry of Health to engage with the whānau of individuals whose case is considered by the CV-ISMB at an extraordinary meeting, especially where there is likely to be a statement from the Board. A meeting between the Chair,

Director NIP and GM Post Event was held on 17 February to discuss this. The NIP (Quality and Post Event Teams) is currently leading on putting this support mechanism in place.

Recommendations

It is recommended that you:

1.	note	The update of the COVID-19 Vaccine Independent Safety Monitoring Board provided in this Memo	Yes/No
2.	note	The Board was reassured with safety data presented for the 5–11-year-olds, however had significant concern around the inequitable roll out and the safety implications of this in vulnerable populations.	Yes/No
3	note	A system is needed for the Ministry of Health to engage with the whānau of individuals whose case is considered by the COVID-19 Vaccine Independent Safety Monitoring Board at an extraordinary meeting.	Yes/No

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

COVID-19 Vaccine Independent Safety Monitoring Board extraordinary meeting – 2 March 2022

Date:	08 March 2022
To:	Dr Ashley Bloomfield, Director-General of Health Astrid Koornneef, Director National Immunisation Programme
From:	Dr John Tait, Chair – COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Decision

Purpose of report

1. This memo seeks to provide an overview of the COVID-19 Vaccine Independent Safety Monitoring Board's (CV-ISMB) meeting held on 2 March 2022 to discuss two fatal reports of concern in individuals following COVID-19 vaccination.

Background and context

2. The CV-ISMB met on 2 March 2022 for an extraordinary meeting to consider two fatal reports of concern:
   - s 9(2)(ba)(ii) [redacted]
   - s 9(2)(a) [redacted] s 9(2)(a) [redacted] who died 8 days after their booster dose of the Pfizer/BioNTech vaccine. The General Practitioner (GP) for this case had indicated that the vaccine response (fever and nausea) could have been contributory.
3. Both cases were previously considered by the Board, with further information sought.
   - s 9(2)(ba)(ii) [redacted]
   - s 9(2)(a) [redacted] was considered by the Board on 9 February; however, a decision on the role of the vaccine was not reached and further follow up information from the GP/s 9(2)(a) [redacted] was sought by the Centre for Adverse Reactions Monitoring (CARM).
4. A study evaluating the effect of the Pfizer/BioNTech vaccine on thrombotic events was also considered by the Board at their meeting on 2 March, following the detection of a potential signal for lower limb thrombosis.

s 9(2)(a)

s 9(2)(ba)(ii)

[redacted]

s 9(2)(a)

13. A second case of s 9(2)(a) who died in the period following vaccination was also considered. The Board reviewed the available information related to this case to determine whether the Pfizer/BioNTech vaccine was a contributory factor.

14. Dr Michael Tatley, Director of CARM presented details of the case, with the initial report and follow up information obtained from the individual's GP. The Coroner was consulted regarding this case, however, did not feel that the death needed to be investigated by them.

15. The Board considers the role of the Pfizer/BioNTech vaccine in the death of this individual unclassifiable. The Board felt that there were other factors that could have contributed and/or caused the events leading to the death and unfortunately these had not been excluded.

16. The Board did not feel that the circumstances of this case changed the known safety profile of the Pfizer/BioNTech vaccine. However, reiterated that it was important for the benefit/risk

for vaccination in the frail elderly to be considered on a case-by-case basis and this was reflected in the Pfizer/BioNTech vaccine data sheet.

Study of thrombotic events

17. Following identification of a potential safety signal for lower limb thrombosis, Medsafe and the Post Event team presented a study to the Board that evaluated the effect of the Pfizer/BioNTech vaccine on thrombotic events.

18. This was conducted as a self-controlled case series, where individuals act as their own control to determine the risk of a particular event.

19. Analysis had shown a statistically significant increased risk for lower limb thrombosis with the Pfizer/BioNTech vaccine, however venous thrombosis showed the opposite, with a statistically significant decrease in risk. As lower limb and venous thrombosis have similar codes, they were combined and there was no signal identified.

20. The Board agreed it appropriate to combine the codes and felt reassured by the data presented, which aligns with international evidence.

Points for note

21. The Board expressed their condolences to the families of both fatal cases considered and emphasised the importance of communication with the family of the s 9(2)(a), especially prior to any release of information related to the case in the media.

22. The Board will not be proactively issuing a media statement in regard to either of the cases considered on 02 March 2022.

23. s 9(2)(a) indicated there was scope for a protocol to define future evaluations by pathologists of potential vaccine-mediated myocarditis as there are a lot of learnings from the case of the s 9(2)(a) and two previous cases in New Zealand. Some of the investigations in these cases would not be routinely conducted/considered and this work would require additional funding.

24. The draft minutes of the meeting are attached for your reference (Appendix 2).

Recommendations

It is recommended that you:

1.	note	Contents of this memo.	Yes/No
2.	agree	For the Programme to scope out the requirements for setting up a defined protocol for pathologists investigating potential cases of vaccine-medicated myocarditis.	Yes/No

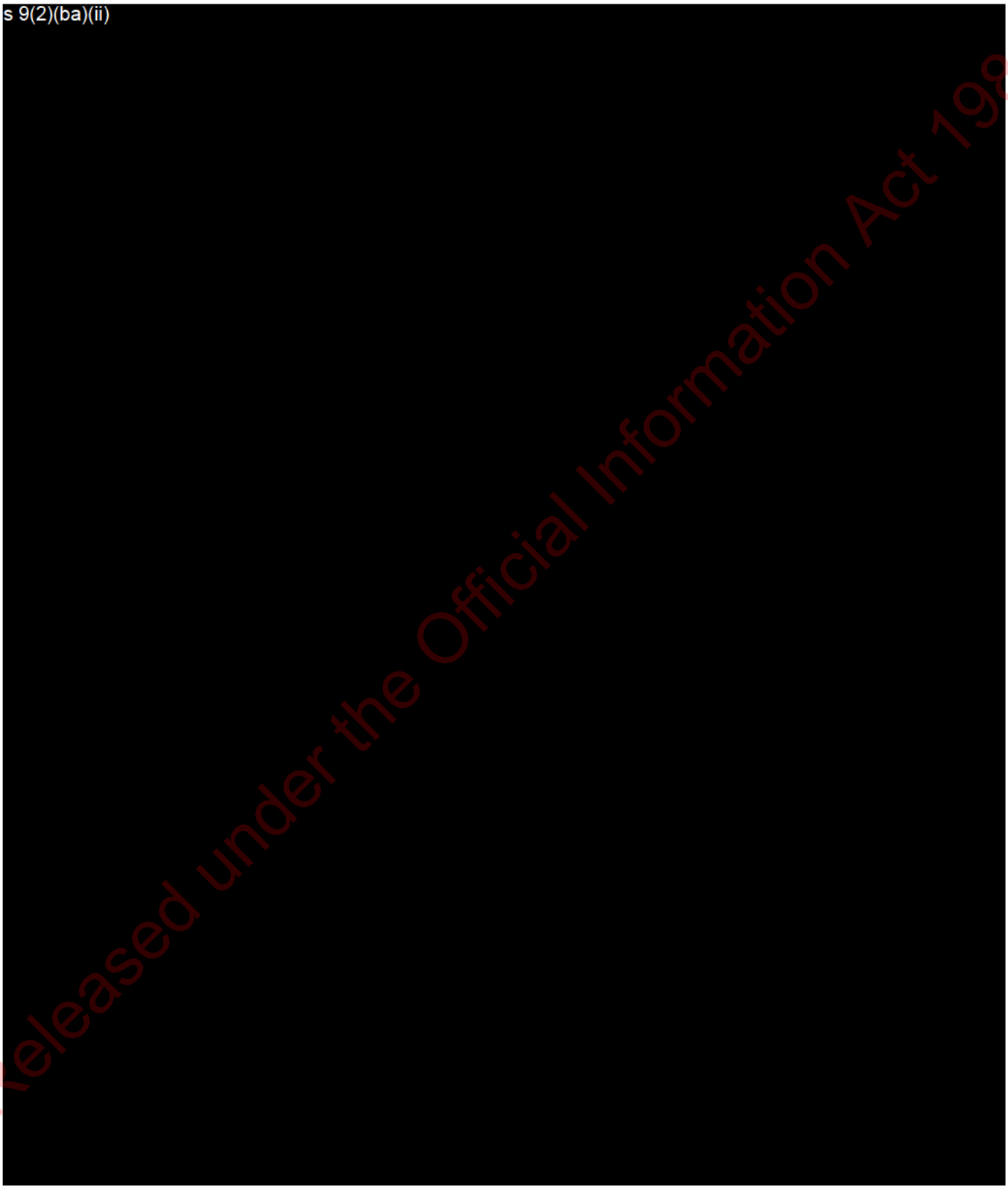
Signature _____ Date:
Astrid Koornneef
Director, National Immunisation Programme

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

Appendix 1

Statement from the Board

s 9(2)(ba)(ii)



Document 11

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

Proactive release of future COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) meeting minutes

Date:	8 March 2022
To:	Dr Ashley Bloomfield, Director General of Health
Copy to:	Astrid Koornneef, Director, National Immunisation Programme Chris James, Group Manager, Medsafe Dr Susan Kenyon, Manager, Clinical Risk Management Branch, Medsafe
From:	Dr Tim Hanlon, Group Manager, Post-Event, National Immunisation Programme
For your:	Action

Purpose of memo

1. This memo seeks your approval to proactively release minutes of all upcoming routine meetings of the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) as approved by the Board Chair.

2. This memo discloses all relevant information.

Summary

3. The CV-ISMB was established in February 2021 to provide expert independent advice and governance in relation to the safety of COVID-19 vaccines in Aotearoa New Zealand to Medsafe, the National Immunisation Programme (NIP, hereafter referred to as 'the Programme'), and the Ministry of Health, in relation to the balance of benefits and risks of COVID-19 vaccines.

4. The Programme's Post-Event Group provides the Board Secretariat. The Programme, Medsafe's Clinical Risk Management Branch, and the Centre for Adverse Reactions Monitoring (CARM) collaborate to provide the CV-ISMB with the latest available information, both domestic and international, regarding COVID-19 vaccine safety.

5. Since its inception, the CV-ISMB has met approximately every 3-4 weeks on a total of 19 occasions to-date.

6. CV-ISMB meetings typically contain content of the following nature:

    i. Discussions around specific cases where there is a temporal association with a COVID-19 vaccine and the likelihood that there is a causal association.

    ii. Expert review of the processes and work feeding into the safety monitoring of the COVID-19 vaccines, such as observed versus expected analysis, rapid cycle analysis and international literature reviews.

    iii. Memos in relation to potential safety signals and safety concerns.

iv. Expert review of individual serious Adverse Events Following Immunisation (AEFIs) reported to CARM, including those with fatal outcomes.

7. Provision has been made for the Board to hold extraordinary meetings to discuss any urgent issue which may arise internationally with regard to the safety of the COVID-19 vaccines or in the event that there is a report of a serious unexpected event in New Zealand, for example a death which may be causally linked to the vaccine. To date the Board has held four extraordinary meetings.

8. There has been increased interest in the CV-ISMB since they released a media statement in December following their meeting on 8 December 2021 around three people who had died with a potential myocarditis in the period following vaccination. OIA requests received have related to the composition of the Board and meeting minutes.

9. To increase transparency around the work of the Board, more information will be published on the MoH website, including the names of Board members, their interim report for 2021 and if agreed, the proactive release of the meeting minutes.

10. The minutes of all CV-ISMB meetings to 15 December 2021 have been requested under the Official Information Act (OIA) 1982 and are due to be released on 8 March 2022.

11. Subject to your agreement, the Ministry will proactively publish future CV-ISMB minutes on its website, beginning with the minutes from 26 January 2022. Requestors for the minutes under the OIA will be directed to the website.

12. To support this process, the Board will approve meeting minutes in the following CV-ISMB meeting and they will then be tabled at Steering Group. They will be published within 48 hrs following Steering Group noting. This will amount to a one-month delay between a CV-ISMB meeting and the publishing of its minutes.

13. Medsafe and the Programme consider that proactively releasing future meeting minutes will provide confidence in the processes of the CV-ISMB.

14. This proactive release would be consistent with the publishing of minutes from other expert safety advisory boards such as the Medicines Adverse Reactions Committee (MARC) meeting minutes on the Medsafe website. The proactive release also mirrors the publishing of Programme cabinet papers due to significant public interest.

15. The Chair and members of the CV-ISMB were consulted about the proactive release of CV-ISMB minutes and agreed in principle to the release at the routine meeting on 9 February 2022.

16. The minutes from the 26 January 2022 meeting in the proposed format for publication are attached as Appendix 1.

Recommendations

17. It is recommended that the Ministry proactively releases the CV-ISMB meeting minutes to instil public confidence in the CV-ISMB and provide transparency around the safety monitoring process for COVID-19 vaccines.

18. It is recommended that future CV-ISMB meeting minutes are formatted to mirror the minutes of MARC meetings which are formatted to provide context for a lay reader to understand the content discussed.

19. If the meeting minutes are not reformatted a large number of redactions would be required which would leave the document highly redacted and inaccessible for a lay reader.

20. A reformatted version would protect any information which falls under the OIA clauses stated below, and would provide context around the discussion to provide an improved reading experience. The OIA allows the withholding of information that:

    a. would breach the privacy of natural persons, including that of deceased natural persons;

    b. is subject to another enactment or could constitute contempt of court (this would include all information that is subject to coronial investigations);

    c. preserves the free and frank expression of opinions by or between or to Ministers of the Crown or members of an organisation or officers and employees of any public service agency or organisation in the course of their duty.

21. It is recommended that extraordinary meeting minutes are not released proactively given that they contain a large amount of information regarding individual persons which is subject to clause 9(2)(a) of the OIA, to protect the privacy of natural persons, including deceased natural persons.

Risks associated with release

22. There is a risk of release of information which must be withheld under the Privacy Act 2020 or information that is subject to another enactment or contempt of court, such as information regarding an ongoing coronial investigation.

23. These risks are mitigated by withholding the necessary content as specified in the OIA.

24. There is a risk in the release of information without the context to explain it as it can be misinterpreted by readers.

25. This risk is mitigated by reformatting the minutes into an improved format for members of the public that articulates topics of discussion and consideration by the CV-ISMB.

Recommendations

It is recommended that you:

1.	Note	The contents of this memo.	Yes
	Note	The reformatting of the minute format to provide context for CV-ISMB discussion.	Yes
2.	Agree	To the proactive release of COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) minutes on the Ministry's website.	Yes/No

Signature _____ Date:

Dr Ashley Bloomfield

Director General of Health

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) tenure

Date:	18 March 2022
To:	Dr Ashley Bloomfield, Director-General of Health Astrid Koornneef, Director, National Immunisation Programme
Copy to:	Chris James, Group Manager, Medsafe Dr Tim Hanlon, Group Manager Post Event, National Immunisation Programme
From:	Dr John Tait, Chair, COVID-19 Vaccine Independent Safety Monitoring Board
For your:	Decision

Purpose of report

1. This memo seeks to provide an overview of the considerations for the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) to continue their work until the future state of the National Immunisation Programme is further defined.

Background and context

2. The CV-ISMB is an independent panel of experts from clinical medicine, microbiology and biostatistics, established to support the review of safety information for the COVID-19 vaccines. The Board provides recommendations and advice to the Centre for Adverse Reactions Monitoring (CARM), Medsafe, the National Immunisation Programme (the Programme) and Ministry of Health.
3. The Board held their first meeting on 25 February 2021 and currently meets every three to four weeks to discuss and review potential safety signals, adverse events of special interest and other reports of note. There is also the provision for the Board to hold 'extraordinary' meetings to discuss a serious unexpected adverse event or issue of concern with urgency.
4. The current membership of the Board stands at 16 with a second paediatrician being appointed in February 2022. Key clinical specialities include neurology, cardiology, haematology and paediatrics, along with representation for both Māori and Pasifika. The Board also holds a position for a lay person to represent consumer interests.
5. In October 2021, the Board's tenure was extended until at least the end of the first quarter of 2022; memo attached as Appendix 1. It has become evident that, with the continued focus on COVID-19 vaccines in 2022, the work of the Board will need to continue past March.
6. An interim report for the Board (February-December 2021) was tabled at Programme Steering Group on 1 March 2022 and will be published on the Ministry website in the next two weeks. This report highlights the importance of the Board's with eighteen safety signals

reviewed and 28 recommendations made to Medsafe and the Programme. In addition, the Board held three extraordinary meetings to consider four fatal reports of note and review emerging data on the concern around thrombosis with thrombocytopenia syndrome with COVID-19 vaccines.

CV-ISMB work in 2022

7. Changes to the Programme, including the introduction of different COVID-19 vaccines, increased eligibility for vaccination and booster doses, require careful monitoring and messaging around safety. To date in 2022, the Board has reviewed:
    - Use of the AstraZeneca vaccine
    - Safety of booster doses in New Zealand
    - Use of the paediatric Comirnaty vaccine
8. The Board has held one extraordinary meeting on 2 March 2022, to consider two fatal reports of concern and review a study evaluating the effect of the Pfizer/BioNTech vaccine on thrombotic events that had detected a potential safety signal for lower limb thrombosis.
9. Medsafe, CARM and Post Event are conducting an observational study to follow up reported cases of myocarditis and pericarditis. Updates on this work are regularly presented and discussed with the CV-ISMB. In addition, Medsafe provides regularly updates on reported cases of myocarditis and pericarditis in New Zealand, along with the international experience for the Board to review and provide feedback.
10. The Board still has a key role in reviewing safety information for the COVID-19 vaccines use in pregnancy including follow up postpartum for congenital abnormalities. This data is evolving as pregnancies are completed and will be ongoing work in conjunction with Medsafe.
11. There remains a need to consider the role of a future Independent Safety Monitoring Board and whether the current CV-ISMB transitions into a National Immunisation Technical Advisory Group (NITAG) beyond the COVID-19 vaccine rollout as the National Immunisation Unit evolves or whether this function is absorbed into the work of the Medicines Adverse Reactions Committee (MARC).

Recommendations

It is recommended that you:

1.	note	The contents of this memo	Yes/No
2.	agree	The CV-ISMB will continue its tenure until at least 30 June 2022 with a further review to be scheduled in advance of that date	Yes/No
3.	agree	That adequate secretariat support will be available to the CV-ISMB	Yes/No

Signature _____ Date:
Astrid Koornneef
Director, National Immunisation Programme

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health