# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 25 February 2021 |
| **Time:** | 4.00-5.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Nick Cutfield, Dr Enver Yousuf, Dr Kyle Eggleton, Associate Professor Matt Doogue, Dr Hilary Longhurst, Dr Tom Hills, Dr Maryann Heather, Dr Anja Werno, Saskia Schuitemaker, Associate Professor Michael Tatley, s 9(2)(g)(ii) [redacted] |
| **Apologies:** | Dr Ian Town, Professor Lisa Stamp, Professor Thomas Lumley, Professor Charis Frampton |
| **Secretariat Support:** | s 9(2)(g)(ii) [redacted] |

| Item | Notes |
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| 1 | **Welcome and Introductions**<br>• Quick introduction from each group member and chair. |
| 2 | **Function of the Independent Safety Monitoring Board**<br>s 9(2)(g)(ii) [redacted] *gives overview of the board and its function.*<br>• This board is independent and will provide advice to key stakeholders, including the COVID-19 Vaccine and Immunisation Programme, Medsafe and the Ministry of Health.<br>• Data must be considered in a programmed way. Ad-hoc advice may be provided, which will require some, or all the board, depending on the case. Advice can be provided to the Director-General.<br>• All members must be sensitive to the emerging adverse event profile. Additional members may be brought in as necessary.<br>• There is potential to feedback significant information into the programme and advise on significant safety concerns. This feedback may significantly impact functionality and programme decisions. Assurance can be provided as necessary.<br>• Thank you from the Director-General for joining the ISMB rapidly. |
| 3 | **Security and Transfer of Data**<br>s 9(2)(g)(ii) [redacted] *outlines the transfer of data process* |

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| | • This board will be working with sensitive health and medical data. It is expected that we respect this data and the need for confidentiality.<br>• A private channel (within Teams) will be set up, to allow sharing of documents and collaborative working in an encrypted and private environment.<br>• Invitations to this environment will follow in due course. s 9(2)(g)(ii) s 9(2)(g)(ii) is available should there be any issues. |
| 4 | **Medsafe introduction and safety monitoring plan**<br>s 9(2)(g)(ii) *explains Medsafe's role*<br>• Medsafe functions to administer medicines legislation and regulate companies. Part of this is pharmacovigilance, to ensure companies are doing the right thing.<br>• This involves three key aspects – signal detection, signal investigation and taking action if needed.<br><br>*Reporting systems relating to COVID-19 vaccine*<br>• Trying to enhance signal detection process. Normally, a spontaneous reporting system (passive system) exists. Anyone can report any suspected adverse reaction which is processed and where needed investigated by CARM who feedback any concerns to Medsafe.<br>• An enhancement of this system is in discussion, to work out a reporting form that is easier for people to use. There is a new reporting tool in the COVID-19 Immunisation Register (CIR) to help vaccinators report anything happening on site. There is work to get an active monitoring system in place.<br><br>*Adverse Events of Special Interest (AESI)*<br>• AESI's help with the investigation and determination aspect.<br>• For the Pfizer vaccine, an AESI we are interested in is the imbalance of Bell's Palsy seen in clinical trials. Working with our IT department, we have found a way to extract data to find out how many cases of Bell's Palsy diagnosed per year in hospital, separated by age and ethnicity. This data will be used to identify any links to vaccination data.<br><br>Periodic safety updates on the Pfizer vaccine are given monthly, so we can identify any adverse events occurring globally.<br><br>The ISMB is critical to determining if any adverse events are coincidental or related to the vaccine. It can then advise what regulatory actions, or other options, are available.<br><br><u>Questions / Discussion</u><br>• Question around the rates of Bell's Palsy that are diagnosed in Primary and Community Care and if this is considered in the Medsafe data. s 9(2)(g)(ii) explains that a study has been commissioned into the background rates of Bell's Palsy in the community.<br><br>**Action** s 9(2)(g)(ii) to see if investigator can do a presentation. |
| | **CARM introduction and engagement with ISMB**<br>*Michael Tatley gives overview of current monitoring system used by CARM.*<br>• CARM has passive monitoring, which is voluntary reporting of adverse events. Its focus is on medicines.<br>• Reports that come in go through a clinical review process, to identify key things (if there is enough data to store in a database, drug/dose relationship, narrative of events, causality and strength of association) |

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| | • Both individual and system issues have potential to drive regulatory functions and can translate into prescribing advice and guidelines.<br>• There is exploration into active systems, as previously it has been passive, sometimes enhanced.<br>• One avenue of investigation is an SMS reporting system, which has been used in Australia since 2009. It functions through an automated SMS sent after a defined period, asking 'Since your vaccination, has anything happened? Followed by several questions and prompts for detail depending on your answer.<br>  ○ Information feedback into a digital system which immediately establishes a database to identify patterns.<br>  ○ About a 70% compliance rate in Australia, with high quality information coming in.<br>  ○ A pilot is due to start and if successful, it could be a good avenue for COVID-19 vaccines.<br>• Specific needs for expertise (from this group)<br>1. Causality review of individual cases of concern (highlight the seriousness of the cases which could have implications for patient and the programme)<br>2. Serious cases of clinical concern. Must determine if it is coincidental, or an AESI<br>3. Identify if the odd events will have system repercussions, despite not being necessarily clinically serious.<br>• Generic guidelines need to be looked at and decide where to provide advice. Advice needs to be constructive. Think about how we translate these discussions into practical advice. |
| 5 | **Any other business**<br>• [redacted] explains how the COVID-19 Vaccine and Immunisation programme must balance the clinical need to have a proper assessment through CARM, but also get ahead of the media interest, which will be heightened following any serious event.<br>• There is a strong desire from within CVIP to test an AESI with a dry run. NZDF will join to ensure proper processes are in place.<br><br>**Action** for [redacted] to send out email regarding payments for the board members. |
| 6 | **Next meeting**<br>• Routine meetings need to be monthly, but next meeting to be held in 2 weeks to discuss guidelines and advice on second dose of Pfizer vaccine.<br><br>**Action** [redacted] to organise poll to identify best meeting time. |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | Thursday 11th March 2021 |
| **Time:** | 3.30-5.00pm |
| **Location:** | Ministry of Health & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Nick Cutfield, Dr Enver Yousuf, Dr Kyle Eggleton, Associate Professor Matt Doogue, Dr Hilary Longhurst, Dr Tom Hills, Dr Maryann Heather, Dr Anja Werno, Saskia Schuitemaker, Associate Professor Michael Tatley, s 9(2)(g)(ii) [redacted] Professor Lisa Stamp, Professor Thomas Lumley, Professor Chris Frampton |
| **Apologies:** | Dr Ian Town |
| **Secretariat Support:** | s 9(2)(g)(ii) [redacted] |

| Item | Notes |
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| 1 | Welcome and Introductions<br>• Two new members welcomed to the group – Thomas Lumley and Chris Frampton. |
| 2 | Meeting minutes<br>• Minutes from last meeting read and accepted. |
| 3 | Medsafe Update<br>s 9(2)(g)(ii) [redacted] *gives update from Medsafe.*<br>• As at 10 March 2021, CARM had received 188 reports of adverse events with the COVID-19 vaccine, 5 of which were considered serious.<br>• 19313 vaccinations completed, with 17 declined vaccinations.<br>• s 9(2)(b)(ii) [redacted]<br>**Action** for s 9(2)(g)(ii) [redacted] to share this report with the group. |
| 4 | Adverse Event Cases<br>*Michael describes two adverse event cases for discussion (detailed in papers uploaded to Teams channel)* |

- s 9(2)(a) [redacted]
- Comments that from a clinical perspective, an important takeaway from these cases is that all have been managed appropriately. However, the group must decide if these cases drive any specific advice. Anaphylaxis is typically rare post-vaccination (of any kind). It sits around 3-5 cases per million. Observed there are currently more in this programme, with 3 reports in 20,000 doses.

**Discussion**

- Well-managed anaphylaxis presents similarly to anxiety and often cannot be confirmed by a clinician. Concerns shared about the paper only noting subjective symptoms.
- Suggestion of defining 'anaphylaxis', for consistency and accuracy of diagnosis. This raised concerns, as anaphylaxis is common for many vaccines (not exclusively COVID-19) and the definition must be able to be applied across the board, in case of a subgroup that responded differently. Suggestions that the definition used standard terminology, is clinician defined, or the use of 'probable' or 'unconfirmed' anaphylaxis. The definition would need to be precise and transparent, to avoid hindering vaccine confidence or conveying more activity in NZ than there actually is.
- Noted that if 'coded' as anaphylaxis in the reporting system, it must meet the criteria of anaphylaxis. An issue was raised regarding what these reactions are called, if not anaphylaxis. Stressed the importance that as a new vaccine with significant public attention, we need to be confident about attributing the actual diagnosis.
- For diagnosis confirmation, it was suggested patients who have an adverse event (hypersensitivity or anaphylaxis) are sent to hospital / medical centre with a leaflet containing recommendations for care, e.g. tests to conduct. A concern was how this information would disseminate to secondary care providers and rural medical practices, who do not always conduct investigations the same as larger hospitals.
- Conducting a tryptase test was suggested, as it would provide more information to make a diagnosis. An IgE test was also suggested, but it was commented that this would be difficult to do early, due to sensitivity. Patients who have an anaphylaxis reaction are referred to immunology, who could do testing in retrospect (except for tryptase).
- The leaflet recommendation was raised as a task for the group. Michael asked the group about if the next vaccine is contraindicated (for this patient) and that a decision is required on the database coding. Stated that 'possible' or 'unconfirmed' isn't an option. Suggestion of a discussion offline to come up with a recommendation.
- Raised that if it is said someone can't have second dose (as they had reaction), then the vaccine excipients would need to be looked into to see if the patient is reacting to any of them, as it may put them at risk for other vaccines.
- Raised that the datasheet is clear in that if you have hypersensitivity reaction, you shouldn't have second dose. Concerned that we have limited information, we are not the clinicians involved and so the group shouldn't be making recommendations on individual cases.
- Questions about this group going forward, specifically the uncertainty regarding detail and number of cases that will be reviewed. Questioned what is required of the group when reviews take place (how it is documented, or do we record if second dose is contraindicated? It was agreed that it is difficult to make specific decisions on individual patients and no one has seen the patient clinically. The group can come up with general recommendations.

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| | • Michael explains there have been other reports, such as hypoglycaemia. He notes that this is the third report with the same presentation. Suggestion to have specific messaging for Type 1 diabetics, due to the number of cases in the last few days.<br>• The group commented that these events are frequent for Type 1 diabetics and should be cautious of labelling type 1 diabetics as 'different'.<br>• Group to note, but no action required.<br>• Agreement that these comments have been valuable, and the discussion is important. Decision to downgrade the reports. |
| 5 | <u>Adverse event follow up process and CV-ISMB process for ad hoc meetings</u><br>s 9(2)(g)(ii) *describes process and use of Microsoft Teams channel.*<br>• Process for ad-hoc meetings is being established.<br>• Feedback received about people not being able to access teams. There is currently work being undertaken with IT to resolve this. Some of the issues are authentication issues, some is due to the use of personal emails. Personal emails are currently not allowed for access to MoH Teams channels. IT are prepared to investigate whether personal emails can be added if issues remain unresolved.<br>• s 9(2)(g)(ii) asked members to email her if they don't have access. |
| 6 | <u>Background rates of adverse events of special interest (AESI)</u><br>s 9(2)(a) *gives overview of AESI current research*<br>• The two key aspects include identifying if you are seeing an increase in events of a particular nature, then you would expect by chance, and having available data when adverse events arise. Issue of separating legitimate events from coincidental ones.<br>• WHO global advisory on vaccine safety have deemed establishing background rates of AESI as an urgent task.<br>• The Brighton SPEAC project have produced a list of AESI (in 4 tiers) developed based on certain criteria: what have we seen in past vaccines that caused concern, what we may see with formulations and if it caused something akin to features of disease. We look at the complete list to see what baseline rates are across age and ethnicity, with Tier 1 prioritised. NZ population is small, which is limiting in helping find rare events.<br>• Compliment this with doing selected chart reviews to get idea of ICD codes that we are going to use.<br>• First output will be Tier 1 AESI. Following this, we can provide some validation of those after doing limited chart review. This is how we will access primary care data.<br><br>**Questions / Discussion**<br>• How long does it take data to get into IDI and when will 2020 data be in there? s 9(2)(a) explained that it varies. Base background rates up to 2019 and 2020 will be looked at separately and hospitalisations run about 6 months behind. However, having done this work before, we can do some rapid cycle analysis if concerns arise.<br>• How reliable is hospital discharge data for conditions that are generally seen in primary care? s 9(2)(a) explains that they are looking at any changes in presentation of hospitalisations and exploring options in how to capture primary care.<br>• Comments that assuming the patient end up in hospital, if that pattern remains the same, you can see the difference.<br>• Discussion around how some conditions are actively managed in primary care, without requiring hospitalisation (i.e. if you develop Bell's Palsy post-vaccination, you are more likely to present to hospital, whereas generally patients present to primary care). There will be greater period of concern post-vaccine as hospital rates are expected to increase. s 9(2)(a) notes that it is currently being worked through.<br>• It was noted how many neurological AESI will present to hospital, but conditions like seizures can be managed without ED presentation. There may be a false positive signal |

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| | through referral process. s 9(2)(a) acknowledges that there is still a lot to work through and it will be iterative process. It will be good to collaborate and compare with other sites internationally.<br><br>• s 9(2)(a) asks the group to advise if there is anything missing, and she will feedback.<br>• s 9(2)(a) suggests that she shares a report (given to the TAG group) to see progress and (at some point) we will have some data to share.<br>• Comments about how the importance of Bell's palsy data from primary care, for interest and important to draw conclusions from, especially if it was publicised as a potential adverse reaction.<br>• s 9(2)(a) comments that the most recent data out from the US, from passive surveillance of 6 million doses, had nothing jump out. Thinks we should keep an eye on this, as initially the rates were well above placebo and baseline rates.<br>• s 9(2)(a) agrees to keep the group updated on progress with primary care. |
| 7 | <u>Potential projects for ISMB</u><br>• Topic areas for discussion include the information training sheet and protocol for hypersensitivity events. Suggestion that the clinical members of the group meet to talk through, then present back to the group. It was questioned what protocols currently exist for anaphylaxis reactions.<br>• It is noted that the attending clinicians will have the same questions and it is up to them to decide how to proceed. Suggested this group produces guidelines, then it is up to the clinicians/ vaccinator's discretion on whether the next dose is appropriate (following anaphylaxis / hypersensitivity event).<br>• Suggestion of a prescriber update article on anaphylaxis and vaccines in general. This was agreed, providing it could be peer reviewed. |
| 8 | <u>Any other business</u><br>• s 9(2)(g)(ii) suggests the next meeting should be held in two weeks (week of 29th March)<br><br>**Action** for s 9(2)(g)(ii) to send out doodle poll to find suitable day for meeting. |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 31 March 2021 |
| **Time:** | 3.30-5.00pm |
| **Location:** | Ministry of Health & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Enver Yousuf, Associate Professor Matt Doogue, Dr Hilary Longhurst, Dr Tom Hills, Dr Anja Werno, Professor Chris Frampton, Professor Thomas Lumley, Saskia Schuitemaker, Professor Lisa Stamp, Dr Owen Sinclair, Associate Professor Michael Tatley, s 9(2)(g)(ii) |
| **Apologies:** | Dr Ian Town, Dr Nick Cutfield, Dr Kyle Eggleton, Dr Maryann Heather |
| **Secretariat Support:** | s 9(2)(g)(ii) |

| Item | Notes |
|---|---|
| 1 | Welcome and Introductions<br>• New member Owen Sinclair welcomed to the group. |
| 2 | Meeting minutes<br>• Minutes from last meeting read and accepted. |
| 3 | CVIP Update: Sequencing and delivery model<br>s 9(2)(g)(ii) *gives overview of the sequencing framework and delivery model.*<br>• The COVID-19 Vaccine and Immunisation Programme, ('The Programme') is rolling out the COVID-19 vaccine through three phases. From July, The Programme will roll out more efficiently, opening the invitation for vaccinations to a broader audience and more locations.<br>• Larger vaccine deliveries are expected throughout Q3 and Q4, so a depletion of all current supply is anticipated between now and the end of June. To keep a steady delivery stream, the rollout slowly scales up to prevent depleting stock early.<br>• From July, there is a significant delivery increase, from 50,000 doses per week to 50,000 per day, reaching around 300,000 doses administered per week.<br><br>**Questions**<br>• Is there is a calculated perceived range of coverage? The model the Ministry operates to accounts for all those being offered a vaccine. Uptake and other factors will determine the actual coverage. |

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| | • Is supply limited until July? The main driver for the first phase is supply limitation. The Ministry is working with District Health Board's (DHBs) and providers to ensure the same workforce is not relied on to deliver both the flu and COVID-19 vaccines.<br>• Is there any modelling to deliver a booster vaccination when we haven't finished vaccinations? No consideration given to this yet.<br><br>• The Programme is working to improve the engagement campaign, system wide delivery strategy, operating model and the logistics and distribution system.<br>• Outlined the sequencing framework, specifying that the Group 1 and 2 are defined populations, which helps manage eligibility while supply is constrained. The general population rollout begins with those deemed high risk, by age and comorbidity. There are people working through how each group will be reached.<br>• Discussed vaccinations for high risk children/ general paediatrics. Until the regulator considers a label change, there are no plans to vaccinate children under the age of 16.<br>  ○ Discussed if there is a need for the vaccine to be used in children, in special circumstances, to deliver a safe outcome.<br>  ○ Pfizer vaccine approval (in the USA) for children aged 12 and over, is expected in August. Trials for children under 12 years old are still in Phase 1.<br>• The group had a split view on the need for off-label use in children, with comments that if there is no evidence of efficacy, exceptions shouldn't be allowed. If there is a strong view from the group, it can be put to COVID-19 Vaccine Technical Advisory Group (CV-TAG) from the Chair. Discussion to be taken offline.<br>• The early vaccine access applications are live and accessible through the Ministry of Health website. Criteria for eligibility is specified on the website, but important to note only adults aged 16 and over are eligible to apply. |
| 4 | <u>Release of CV-ISMB information</u><br>• There is significant interest in the vaccine rollout and consequently, The Ministry has received a number of OIAs and media queries regarding this group. To provide assurance and a transparent approach, The Ministry intends to publish names and bios of each group member on the Ministry of Health website, similar to MARC committee<br>• Group agrees to publish names and short bios on the Ministry of Health website.<br>• **Action for** s 9(2)(g)(ii) to send draft response to all members to check details. Each member will provide a short paragraph with their background information. |
| 5 | <u>CV-ISMB purpose and function</u><br>• A deputy-chair is required for the ISMB. The group will take nominations, or members can contact s 9(2)(g)(ii) directly if interested.<br>• This group functions to ensure the Ministry of Health has well resourced, professionally orientated safety advice.<br>• Dr Ian Town provides link between CV-ISMB and CV-TAG. He is non-voting member.<br>• The chair will work with the Director-General, Dr Ashley Bloomfield and National Director CVIP, Jo Gibbs, to raise issues and concerns after each meeting. |
| 6 | <u>CVIP Safety Update</u><br>s 9(2)(g)(ii) *gives update.*<br>• Around 60,000 doses have been administered, with Counties Manukau DHB administering the most vaccinations to date.<br>• 506 AEFI events have been reported, of which 491 were non-serious and 15 serious.<br>• An expected spike in reports was observed at the beginning of the rollout. This has settled to a plateau, with the reporting rate sitting at around 0.8%.<br>• The serious reports received include – angioedema, seizure (mild jerk), dyspnoea, throat tightness, chest tightness (which can also be anxiety or hypersensitivity) and anaphylaxis.<br>• The highest reported reactions are dizziness, headache, nausea, fatigue and fever. |

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| | • General reports received through the COVID-19 Immunisation Register (CIR) are hypersensitivity and anxiety. The number of reports submitted through CIR is decreasing as vaccinators become more confident. The number of reports submitted to CARM is increasing, especially as more people receive their second dose.<br>• The Ministry is aware no safety data has been published to date. There is political concern surrounding how this data will present. The Ministry is working through how not publishing the data initially could imply a high rate of adverse events and safety issues and are actively encouraging the data to be published.<br>• A draft of the proposed data webpage is shown. The webpage includes most commonly reported events and a dashboard. s 9(2)(g)(i) [redacted]<br>• Medsafe have just published the Comirnaty risk management plan which includes an overview of studies Pfizer will undertake and have completed.<br><br>**Questions**<br>• Is the total AEFI reports the best denominator? Would number of doses administered be more appropriate? Both totals are included on the dashboard. The vaccine event occurs quickly, but the number of reports come in over time, with the possibility to receive reports months later.<br>• Comment that one must be strict on what determines a serious event. Explained that internationally agreed criteria states that if an individual is admitted to hospital after an adverse incident, it is considered a serious event. |
| 7 | <u>Anaphylaxis and hypersensitivity proposed documentation</u><br>• Following the discussion at the 11 March meeting around whether specific adverse events were anaphylaxis, a document has been drafted, with a checklist for anaphylaxis based on the Brighton Criteria.<br>• Its purpose is to be used when an adverse event occurs, allowing for a record to be kept and assisting to determine if the suspected case fits the definition. It could assist ED and CARM with obtaining necessary information for reporting.<br>• As the rate of anaphylaxis is low, an event should not be over-diagnosed.<br>• The document should be supplemented with an outline of the protocol for clinics, and a reporting protocol for how the data is evaluated.<br>• Guidelines surrounding what a hypersensitive or vasovagal event is, could be provided to vaccination sites. CARM has received a number of questions from nurses and GPs asking about whether certain events are significant. Non-regulated vaccinators may be used in the later phases of the rollout and may benefit from guidelines. This could be furthered by guiding whether a second dose is appropriate, using subjective or objective symptoms.<br>• The group had comments on this process, including that it shouldn't be oversimplified, as the system is complex and raising the issue of whether vaccinators have sufficient time to complete the form post-event, or whether they would be able to capture everything at only this point.<br>• Personal Information and CARM: CARM often receives a significant level of patient information and confidentiality is always maintained.<br>• Suggestion that a memo is written, supporting the documentation but noting the importance of determining the diagnosis so a decision can be made on whether a second dose is contraindicated. The memo will raise the issue of inadequate information feeding into CARM (to allow for classification of events). It will explain the requirement for a clinical pathway for consumer's who experience these events acknowledging different services in different parts of the country. Noted there is one part of the memo for CVIP and one part for CV-TAG. |
| 8 | <u>Clinical management of complex cases</u><br>*Matt Doogue explains the importance of clinical management* |

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| | • There is importance in determining the diagnosis of adverse events, to ensure clear advice is given and a decision can be made on whether second dose is contraindicated.<br>• An issue identified is that DHBs are yet to create a model for identifying patient's pre/post first vaccine. Has engaged in conversations with a limited number of DHBs on this model. The Ministry of Health will assist with commissioning pathways.<br>• The pathway needs to include the issue of support for complex cases. To date, individuals of concern have been identified by CARM through the AEFI reporting process. The clinical pathway will be commissioned and reviewed by the Ministry of Health, putting it forward as a model for adoption.<br>• The DHBs and ISMB need to come up with a process and present to CV-TAG for next steps.<br>• Comments that it is impossible to judge whether information contained makes any guidance on if second dose is contraindicated. It is important to find a solution that works across country, and in patient's best interest.<br>• Suggests contraindications are recorded based on traditional methods. Believes it causes a clinical risk given the absence of information. s 9(2)(g)(ii) notes that as the programme scales up, we need to clearly separate the pharmacovigilance process from clinical pathway design and support to DHBs.<br>• Fundamentally, it is to ensure a safe process exists where an individual can receive the vaccine, taking into account the goal is to vaccinate as many individuals as possible. |
| 9 | <u>CV-ISMB ad hoc meeting process</u><br>• Process to bring group together at short notice is required, in the event of two circumstances:<br>  ○ Urgent issue overseas<br>  ○ Serious unexpected event – for example a case has approached the media, or a cluster of deaths where further information and advice is required.<br>• Although it is unlikely this process will be used, it needs to be tested for confidence in the process. s 9(2)(g)(ii) will plan a test run.<br>• Ensure that everyone has access to teams (to share information securely).<br>• Some members will be vital to the meeting, depending on the issue. Those deemed essential need to be contactable via phone.<br>• **Action for** s 9(2)(g)(ii) to collect all members contact details. |
| 10 | <u>Any other business</u><br>• Next meeting to be held in approximately one month's time.<br>• May conduct a trial ad-hoc meeting during this time. Will circulate final documentation once complete.<br>• Raised that in Terms of Reference of group, members should be looking at international safety reports. Request to be sent international reports.<br>• **Action for** s 9(2)(g)(ii) to provide reports in Teams channel. |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 29 April 2021 |
| **Time:** | 3.30 - 5.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Enver Yousuf, Dr Hilary Longhurst, Dr Tom Hills, Dr Anja Werno, Professor Chris Frampton, Professor Thomas Lumley, Saskia Schuitemaker, Professor Lisa Stamp, Dr Owen Sinclair, Dr Maryann Heather, Associate Professor Michael Tatley, s 9(2)(g)(ii) s 9(2)(g)(ii) Dr Ian Town, s 9(2)(g)(ii) |
| **Apologies:** | Dr Nick Cutfield, Associate Professor Matt Doogue, Dr Kyle Eggleton |
| **Secretariat Support:** | s 9(2)(g)(ii) |

| Item | Notes |
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| 1 | **Welcome and Introductions**<br>• Minutes of 31 March read and accepted.<br>• Request for the minutes from 22 April to be amended.<br>  ○ s 9(2)(g)(ii) has asked for feedback on proposed amendments by close of business Friday, before the final minutes go to Steering Group next week. |
| 2 | **Immunisation Advisory Centre overview**<br>*Dr Nikki Turner gives overview of IMAC and its role alongside the Ministry.*<br>• The Immunisation Advisory Centre (IMAC) runs immunisation coordination across New Zealand. Additionally, they run educational training programmes and provide clinical advice. The Ministry is able to ask IMAC for advice. IMAC runs a phone and email line which provides clinical advice for any healthcare provider. Any particularly tricky Healthline questions are directed to IMAC.<br>• Currently, the phone lines are managed by nurses and clinical advisors. IMAC has a working relationship with the Centre for Adverse Reaction Monitoring (CARM). The volumes of calls will become increasingly challenging as vaccinations administered increase for the COVID-19 vaccine. |

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| | • IMAC are looking to set up virtual clinics with providers, drawing on experts (for example, neurologists and immunologists) if required.<br>• The COVID-19 Immunisation Register (CIR) has good functionality to record any adverse events following immunisation. District Health Boards are looking at this data for consideration of second doses and IMAC is working with Auckland DHB to help with a national approach. |
| 3 | **CV-TAG Overview**<br>*Dr Ian Town gives overview of the COVID-19 Vaccine Technical Advisory Group*<br>• Medsafe retain independent advice on safety of the vaccine or pausing programme.<br>• The COVID-19 Vaccine Technical Advisory Group (CV-TAG) is part of the COVID-19 Vaccine Strategy Taskforce. Initially this taskforce led to the formation of the Science and Technical Committee, which led to securing four Advance Purchase Agreements (APA) from a suite of vaccines. Following this, MBIE's work was migrated over to the Ministry of Health.<br>• CV-TAG has members largely comprised of the COVID-19 Vaccine Taskforce, with additional clinical support. The group provides advice and guidance to the Ministry of Health COVID-19 Vaccine and Immunisation Programme (CVIP) National Director. CV-TAG is approached for advice on technical, scientific and clinical advice, which CVIP then operationalises.<br>• IMAC representative sits on CV-TAG to provide sit rep on current status and to provide advice to sector to ensure any issues are mitigated.<br>• Work is required to streamline communication between CV-TAG, Immunisation Implementation Advisory Group (IIAG) and ISMB, as there is a significant overlap in activity. Additionally, it will help to keep everyone informed to avoid miscommunication.<br>• No discussion from group. |
| 4 | **Steering Group memo update**<br>s 9(2)(g)(ii) *gives update on the memo from 31 March meeting*<br>• The memo submitted by the ISMB was reviewed by Dr Ian Town and Jo Gibbs, provided feedback that the anaphylaxis checklist was recommended as an addition to the programme. This feedback will be incorporated into the updated memo submitted to Steering Group.<br>• Contraindication of second dose and management of consumers who have had AEFI was discussed at CV-TAG and s 9(2)(g)(ii) has been asked to facilitate a working group to design a protocol for DHB and Clinical Lead feedback.<br>• CV-TAG also discussed specific questions raised by ISMB:<br>  ○ *Consideration of vaccinations for high-risk paediatrics*. It was decided that vaccinations in children aged under 16 is not justified. This aligns with the label given.<br>  ○ *Modelling for potential of booster vaccination*. Noted by Chair and item will be added for point of further work in the future.<br>• No discussion by group. |
| | **AEFI Case Reports update**<br>*Michael Tatley gives update on anaphylaxis cases and other cases of note*<br>• The Centre for Adverse Reaction Monitoring (CARM) has received 8 cases of reported anaphylaxis, as selected on CIR by the reporter.<br>• Questioned the group on what level of detail is required on a per-case basis. Proposed to highlight anaphylaxis cases and put aside for process discussion, where they can be analysed in greater depth. There will be more cases reported (when tick box is selected |

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| | on CIR) which may not fit the criteria. The discussion on detail and subsequent process to be continued at a later time.<br>• High-level overview of each case provided in **Appendix One.** Important to note that all cases have been treated appropriately clinically. Each case has been assessed and assigned a Brighton Criteria (BC) level.<br>• Recording events in database allows reporting of anaphylaxis, but also the application of a BC level. It is a more useful way of looking at cases and considering when we report. Useful to have a further perception of what is thought to be an appropriate BC level.<br>• Other jurisdictions publish data similarly. Open to discussing each case and means of validating application of BC. The current reports are narratives presented to CARM by reporter.<br><br>Discussion:<br>• Comment around the current reports being a classic distribution of reactions defined as anaphylaxis, from typical L1/L2 through to unlikely anaphylaxis cases. Noted it is helpful to collect information to gather certainty. A checklist tool will streamline this process, assisting to identify the BC level. Additionally, it helps to compare to reports overseas. Reports support efforts to establish checklist.<br>• Comment that as the number of vaccinations administered increases, there will be an increase in hypersensitivity reactions. A need is not identified to assess individual cases but acknowledge that anaphylaxis is being reported and managed appropriately. Comment about whether it is ISMB's job to determine if cases are anaphylaxis or not, and to be wary of looking at individual cases as will get caught in the detail.<br>• Discussion surrounding the proportion of people receiving their second dose, and whether there are any indicators to look for. There are increasing numbers of second dose reports, with no clear indicators except for the reaction profile is more severe or profound for individuals and persists for longer period of time.<br>• Comment on the usefulness of CARM to have background rates of myocarditis. s 9(2)(g)(ii) s 9(2)(g)(ii) explained that the Qlik app, which provides data on background rates of disease, has an acute cardiovascular injury section, including the rates of pericarditis and myocarditis. Acute myocarditis is the best comparison (rather than infective myocarditis), with a total of 58 occurrences, 48 of which were principal diagnoses. It is more common in 18-44-year-old men.<br>• Noted that it may be useful for group to consider, if between meetings, myocarditis becomes a larger concern internationally. s 9(2)(g)(ii) comments that Medsafe have begun a signal investigation and the rates match the Israeli pattern perfectly, as the case in question occurred after the second dose.<br>• Question about how myocarditis would be coded post-vaccination, or how it is generally coded in the absence of vaccination. As infective myocarditis is rare, it is unclear what this would be coded as in the absence of vaccination.<br>• Suggestion from s 9(2)(g)(ii) to seek cardiologist expertise. s 9(2)(g)(ii) asks for recommendations for a cardiologist with experience in dataset coding.<br>• Comment that for case 11, the working diagnosis is myocarditis, but a final diagnosis is yet to be determined. CARM is awaiting the hospital summary. |
| 5 | **Medsafe update**<br>s 9(2)(g)(ii) *gives Medsafe Update and demonstration of Qlik AEFI app*<br>• s 9(2)(g)(ii) shows the dashboard of AEFI, with breakdown of daily and weekly cases available. Events are reported in medical terms, by which some events have no coding.<br>• Important to note that 'Adverse events' means case numbers, rather than report numbers (as can be double reported). |

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| | • Currently, the most common side effect is headache.<br>• Figures are not entirely accurate currently due to issues with the application.<br>• There are many important features of the app, including being able to filter the data by demographics (ethnicity, age, gender, deprivation quintile)<br>• There are new pages, including the rate of AEFI, and time-to-onset of AEFI. There is also a filter of MedDRA terms, which could be useful in identifying signals. Additionally, there is information about the report itself, such as source of report, severity level and reporter type (such as vaccinator or nurse)<br><br>Discussion:<br>• Group pleased with platform, despite the current glitches.<br>• Question around where the data comes from. It is a platform that is collating data from all reporting aspects, such as CARM website, CIR, traditional CARM reporting and paper-based reports. All reports are validated from a CARM perspective, as Michael is able to access all reports, including CIR data.<br>• Comment about access to oxygen in resus room within vaccination sites. s 9(2)(g)(ii) to raise issue within the Ministry CVIP team and discuss offline. |
| 6 | **Any other business**<br>• John requests any feedback or issues from the ISMB committee, to present to the Steering Group on 11 May.<br>• Michael asks if the reporting type is suitable for the group and for any suggestions of additional information required at an individual case report level. Chair notes Michaels valuable contribution.<br>• s 9(2)(g)(ii) asks for feedback on the timing of regular meetings, including whether monthly frequency is working. Ad-hoc meetings may need to be after hours.<br>  ○ If monthly meetings are suitable, s 9(2)(g)(ii) will aim to get calendar invites out early to plan in advance. Comment that as vaccination numbers increase, meetings may need to increase as well. However, monthly works for now.<br>Meeting closed. |

s 9(2)(a)

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 27 May 2021 |
| **Time:** | 3.30-5.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Nick Cutfield, Dr Enver Yousuf, Dr Hilary Longhurst, Dr Tom Hills, Dr Maryann Heather, Professor Chris Frampton, Professor Thomas Lumley, Saskia Schuitemaker, Dr Owen Sinclair, Associate Professor Michael Tatley, s 9(2)(g)(ii) s 9(2)(g)(ii) Dr Ian Town |
| **Apologies:** | Dr Anja Werno, Associate Professor Matt Doogue, Professor Lisa Stamp, Dr Kyle Eggleton |
| **Secretariat Support:** | s 9(2)(g)(ii) |

| Item | Notes |
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| 1 | **Welcome and Introductions**<br>• Minutes of 29 April meeting accepted.<br>• Steering Group memo update: Consideration on anaphylaxis checklist agreed and given to s 9(2)(g)(ii) to operationalise.<br>  ○ s 9(2)(g)(ii) working to implement at a site-level and determining whether form will be used through the COVID-19 Immunisation Register (CIR) or be paper-based.<br>  ○ s 9(2)(g)(ii) will provide update at next meeting. |
| 2 | **Polynesian Support**<br>*Update from Global Health by* s 9(2)(g)(ii)<br>• There will be an amendment to the Terms of Reference (TOR) for the ISMB, to allow for support to be provided to Realm countries in the first instance, as well as Samoa and Tonga.<br>• First vaccines were rolled out in Cook Islands on 17 May in Rarotonga, with extension to outer islands occurring in the next six to seven weeks. 6000 vaccinations completed since 17 May, with 12 non-serious adverse events following immunisation (AEFI) reported so far, and zero serious. |

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| | • The reporting system has been enhanced so countries can provide data to NZ and CARM can assist with medical assessment.<br><br>Discussion:<br>• Question on the ability to discuss a significant adverse reaction with clinicians in the Cook Islands and reassurance provided that there are two clinical leads available for possible discussion via telephone. Additionally, the Immunisation Advisory Centre (IMAC) are working in counties or remotely to provide online training regarding serious/non-serious AEFI management.<br>• Noted there is a long-term approach under consideration around pharmacovigilance monitoring in the Cook Islands.<br><br>**Action for** s 9(2)(g)(ii) to send amendments to the TOR to the group for consideration and approval. |
| 3 | **CVIP Clinical update**<br>s 9(2)(g)(ii) *gives clinical update*<br>• The COVID-19 Vaccine and Immunisation Programme (CVIP) Clinical Quality and Safety team is comprised of clinicians, who are tasked with providing clinical advice across workstreams as required, as well as governance and stewardship.<br>• A gap identified is workforce monitoring quality, particularly as new workforces are involved.<br>• Currently working to develop a clear set of standards to be applied across any setting for providers. They have also established a National Quality and Safety forum which meets fortnightly to monthly to provide governance. Potential to combine with ISMB to work together to cover entire programme and discuss quality.<br><br>Discussion<br>• Comment that it is good to see how everything fits together.<br>• Comment about workforce issues, specifically the troubles to get enough vaccinators on site and issues with second dose bookings. Noted that it is helpful to hear feedback and that hopefully the booking system being rolled out will resolve some issues. |
| 4 | **Cases of Significance**<br>*Michael Tatley gives update of AEFI over previous month*<br>• There have been three reports of death in individuals who have received a COVID-19 vaccine, all of which have been found to be unrelated to the vaccine and instead due to underlying or other conditions.<br>• Noted there needs to be some consideration given to communication about comorbidities.<br>• There have been numerous other cases of note including a TIA, which was unrelated to the vaccine, as well as DVT, Bells Palsy and lacunar infarct stroke, as outlined in the AEFI report.<br>• s 9(2)(a) [redacted]<br><br>Discussion:<br>• Comments that lacunar infarct stroke is very common and often occurs in people average 70 years old, and those with perivascular disease, hence is not too significant. |

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| | • Question about the patient who experience nephrotic syndrome and whether they take any over the counter medications. Michael to chase up, as it appears patient was otherwise well.<br>• Comment that the other stroke case is potentially interesting, and that more information is required to establish if there is a relationship with the vaccine or not, specifically if there were any risks for venous clotting in the individual.<br>• Comments about not being to concerned regarding seizures, especially if the individual does not have perfectly controlled epilepsy prior to vaccine and are on different doses of topiramate. Similarly, for Bells Palsy, it can be mild and recover quickly, meaning individuals may not get to the point of presenting to GP. The numbers depend on baseline incidence data which can be difficult to establish without primary care data.<br>• Noted that it is relevant for all cases to have the background rates.<br><br>*Anaphylaxis reports*<br>• Outlined how CARM are continuing to receive reports of anaphylaxis and that it was agreed to apply the Brighton Criteria (BC) against each case that has been reported as anaphylaxis.<br>• Raised that New Zealand has currently reported roughly 18 anaphylaxis cases for approximately 600,000 doses and whether this represents the true rate, as Pfizer data indicated three to five cases per million. Questioned whether it is worthwhile to do an audit on whether it is being reported at the right level, as we are getting higher numbers than international data.<br>• Important to note that serious AEFI reports are very low.<br><br>Discussion:<br>• Group not as concerned regarding increased rate of AEFI as New Zealand may have better reporting rates than other parts of the world. Additionally, many anaphylaxis reports are low level BC and it is early days of the programme with high scrutiny.<br>• Further discussion that our rates of AEFI are higher as we have a good system of reporting, which is focussed and primed on finding events. There will always be rates of AEFI, but as long as it isn't very common. We don't want to be over-diagnosing or over-applying the BC.<br>• Comment that some anaphylaxis events are happening hours after the event and as such, if we want to assign casualty we need more information. We should be looking into details for those events as level one and two. |
| | **Signals**<br>*Medsafe gives update on signals*<br>• Herpes zoster reactivation<br>  ○ Incidence in New Zealand is similar to global estimates. So far, New Zealand has seen 7 cases of shingles reactivation following Pfizer COVID-19 vaccine. Important to note that all cases followed first dose and are usually in people aged 50 and over.<br>  ○ This is not just seen in Comirnaty, it has been seen in other COVID-19 vaccines, with Moderna reporting the lowest rate as it has been administered the least compared to other vaccines.<br>  ○ Medsafe are proposing to continue monitoring rates through routine pharmacovigilance. Pfizer are submitting PSUR (currently submitted monthly) as a topic for consideration and will be looking at available data.<br>  ○ Asked the group if they would like to make any additional recommendations to Medsafe. |

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| | ▪ Group commented that the proposal through routine pharmacovigilance is valid and a good way forward. No additional comments.<br>• Appendicitis<br>○ Memo based on case identified in New Zealand. A Swedish prepared report found some unexpected numbers of appendicitis. Highest rates of appendicitis generally occur in younger people, who we are not currently vaccinating.<br>○ More cases found with Pfizer than Moderna.<br>○ Appendicitis is included in label, as reported in datasheet.<br>○ Not currently thought of as a signal, with recommendation from Medsafe that it is continued to be monitored and wait for PSUR for May.<br>○ Discussion:<br>▪ Whether appendicitis is related to histology or abdominal pain. There was incomplete information for many cases, as is normal for spontaneous reporting.<br>• Myocarditis<br>○ Medafe will be receiveing more data soon (i.e. from Israel). Currently, hospital data is being collected.<br>○ Questioned group on if there is enough evidence to support connection between Comirnaty and myocarditis, as well as if any communication is required (and to who?).<br>▪ Comment that there may be a connection and that it is a signal that requires investigation. The rate seems to be low based on reporting and on the memo.<br>▪ Unsure if Medsafe have already put out a monitoring communication, but if not, it needs to be worded in a reassuring way. It would be best to monitor communication through the usual channels. |
| 5 | **Medsafe update**<br>s 9(2)(g)(ii) *gives Medsafe update*<br>• Majority of cases reported are non-serious. Headache is still the most reported commonly adverse event. There is a large difference in the number of reports between male and female, which is partially reflected in who is currently being vaccinated as well as females are generally better at reporting.<br>• Slight downward trend in reporting rate, and it is normalising against populations being vaccinated. |
| 6 | **Any other business**<br>• Matt forwarded an email to group about concern regarding amber test results for those taking clozapine and receiving COVID-19 vaccine. There is work underway with IMAC and s 9(2)(g)(ii) about this.<br>• Comment regarding the absence of discussion on equity in the group and within the TOR<br><br>**Action for** s 9(2)(g)(ii) to follow up with s 9(2)(g)(ii) and provide update to group about Clozapine and receiving vaccine.<br>**Action for** s 9(2)(g)(ii) to invite an equity team member to next meeting.<br><br>Meeting closed. |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 24 June 2021 |
| **Time:** | 3.30-5.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Enver Yousuf, Associate Professor Matt Doogue, Dr Hilary Longhurst, Dr Tom Hills, Dr Anya Werno, Professor Chris Frampton, Professor Thomas Lumley, Saskia Schuitemaker, Professor Lisa Stamp, Dr Owen Sinclair, Dr Nick Cutfield, Dr Kyle Eggleton, Associate Professor Michael Tatley, s 9(2)(g)(ii) s 9(2)(g)(ii) |
| **Apologies:** | Dr Maryann Heather, Dr Ian Town |
| **Secretariat Support:** | s 9(2)(g)(ii) |

| Item | Notes |
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| 1 | **Karakia and Welcome**<br>• Meeting minutes from 27 May read and accepted. |
| 2 | **Medsafe memos**<br>*Stroke following Comirnaty*<br>• CARM has received a total of 11 stroke cases post-vaccination, 3 haemorrhagic, 4 ischaemic and 4 other or unspecified. There have been strokes reported by other regulators, but it is currently not recognised as an adverse drug reaction (ADR). However, it is being observed closely as an adverse event of special interest (AESI).<br>• We are seeing a significantly smaller number of reported strokes than what is expected in comparison with background rates.<br>• s 9(2)(ba)(ii)<br>• Medsafe propose to continue routine monitoring and asked the group for any additional recommendations.<br>  ○ Query as to why the rates are so low in comparison to background rates. Explained that as it is very early days in the programme, not all population have been vaccinated yet. |

- Comments that the numbers are reflective of the low number of people vaccinated so far and that there hasn't been a spike, which would be concerning. There is also no particular phenotype or pattern to the cases.
- Comment that it would be useful to be explicit about denominators in order to give an accurate comparison, as total population vs vaccinated population is contrasting.
- Overall, the group agreed with Medsafe and had no further advice.

*Myocarditis following Comirnaty*

- New information from CDC today provided early safety data for young people aged 12 to 15. There are slightly less reactions occurring for younger age group, with more reactions occurring following the second dose.
- Young males are experiencing higher rates of myocarditis than expected for the 12-24 years (significantly higher) and 25-39 years (slightly higher) age groups. Females are also seeing a higher rate of myocarditis following the second dose in the 12-24 years age group, but this is not as pronounced as the difference observed in males.
- A rapid cycle analysis has been completed for Moderna and Pfizer for the adverse reactions of myocarditis/pericarditis. The benefits clearly outweigh risk.
- Medsafe propose to continue routine monitoring. No discussion from group.

*Menstrual disorders following Comirnaty*

- There have been reports of unexpected vaginal bleeding following vaccination.
- There is considerable public interest in this topic.
- There are several medical uterine bleeding disorders. There is a certain amount of variability in one's menstrual cycle, and it can change relating to stress and other lifestyle factors or underlying medical conditions. These disorders are relatively common and are a very small subset of types of reports reported to CARM.
- There have been 22 reports submitted as at 22 June, compared to 500,000 vaccinations administered so far. Most reports submitted by patients and are reported as mild.
- s 9(2)(a) [redacted].
- The summary in the monthly safety report stated that abnormalities were reviewed and determined not to be a safety signal.
- Volume of reports received is not unexpected and so Medsafe propose to continue monitoring through routine pharmacovigilance.

Discussion:

- Comment that no individuals were hospitalised that numbers are expected. It is plausible they are linked but more data is required.
- Group agree to continue to monitor.
- Comment about removing adverse event reports from people who have not yet received the vaccine. Michael explains that people can report without having the medicine and that it cannot be removed from the system but can be marked as invalid.

*Pancreatitis following Comirnaty*

- s 9(2)(a) [redacted].
- s 9(2)(ba)(ii) [redacted]

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| | • Background rates indicate there are 50 cases per 100,000 per year in age group. Idiopathic cases represent 10-15%. NZ study shows incidence in Maori is significantly higher than European in every age group.<br>• Medsafe suggest monitoring as per normal pharmacovigilance.<br>• Discussion<br>  ○ s 9(2)(a) [redacted] |
| 3 | **Equity**<br>• There is no mention of the Treaty of Waitangi or equity in the ISMB Terms of Reference (TOR).<br>• There is a need for inclusion as Māori are at higher risk of all COVID-19 related incidents, including side effects of the vaccine.<br>• There will be signals that Māori experience higher than European populations. The group discusses a lot of individual cases but not much at a population scale. A population at risk may need a different approach to identified signals.<br>• s 9(2)(g)(ii) [redacted] is working to incorporate equity considerations into the TOR.<br>• Discussion<br>  ○ Group agree there was an oversight in the TOR<br>  ○ In terms of data collection, confirm that there is reporting by ethnicity.<br>  ○ Comment that if Māori are not reporting at higher rates then there is reason for concern.<br>  ○ Agree to get members of the Ministry COVID-19 Vaccine and Immunisation Programme (CVIP) equity team to speak at a meeting.<br><br>**Action for** s 9(2)(g)(ii) [redacted] to work with Data and Analytics team to provide regular reporting for group. |
| 4 | **Overview of fatal reports**<br>*Michael and* s 9(2)(g)(ii) [redacted] *overview of fatal reports*<br>• CARM have received a number of reports of death in vaccinated frail elderly. The CVIP National Director has asked Ian Town to work with s 9(2)(g)(ii) [redacted] the CVIP Clinical team to implement any clinical guidance around vaccinations for the frail elderly. This has ethical and practical clinical considerations. There will be a request for literature and guidance from other countries and the guidance will be presented to CV TAG.<br><br>Discussion:<br>  ○ Comment to be careful about attributing death due to natural causes to those in frail elderly. In the elderly, frailty is defined as a decrease in physiological reserve across multiple organ systems leading to increased vulnerability to even seemingly minor external stressors; it is possible that an immunological response to any vaccination is a physiological stressor.<br>  ○ Comirnaty has not been studied in elderly frail population in clinical trials, although there is now some real world data. The group must be cognitive of this information when reviewing death in the elderly.<br>  ○ Concerns about the appropriateness on vaccinating elderly people with a terminal illness and/or where health is in decline. |

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| | • Brief summary of deaths that have occurred over the last month. Many have occurred in extreme elderly and some have been in advanced dementia type situations, or pre-terminal.<br><br>Discussion:<br>• s 9(2)(a) [redacted]<br>• Agree with discussion regarding elderly that on the balance of probabilities, these people are very sick and often pass away of non-COVID related illnesses. However, may also experience vaccine related ailments.<br>• Question around whether extra investigation could be undertaken for those otherwise vulnerable, especially for those prone to COVID-related illnesses.<br>• Comment that PVT is expected in those near-terminal and not uncommon in chronic liver disease.<br>• s 9(2)(a) [redacted]<br>• General comment about how stroke and CVA reporting is poor. There is a limitation to what people report.<br><br>*Anaphylaxis reports*<br>• The current agreement with group rather than looking at each case in detail, Michael will assign the Brighton Criteria (BC) and report the list.<br>• There appears to be a higher rate than what is reported elsewhere; noted that the Brighton criteria may be oversensitive in the absence of full immunological evaluation.<br><br>Discussion:<br>• Found the data reassuring, as initially we appeared to have higher rates than overseas.<br>• Report highlights the ability of the BC. Only levels 1-3 would be considered true anaphylaxis, and these rates are similar to the CDC. New Zealand may see higher rates as there is a robust report system<br>• Suggestion to only bring anaphylaxis reports to meetings if a spike is seen.<br>• Group agrees to bring anaphylaxis reports back if there is any raised numbers or unusual cases. Data will be left with CARM. |
| 5 | **Reported Cases**<br>• A few cases of hypoglycaemia in type 1 diabetes that were uncontrollable. Flagged as a potential topic of interest.<br><br>Discussion:<br>• s 9(2)(a) [redacted]<br>• Brief comment about Guillain-Barre syndrome and whether it was first or second dose. Doesn't seem like sufficient time to generate an immune response.<br>• Comment about seizures and the duration of convulsions. Time is often overestimated by witnesses and non-epileptic seizures can happen following procedures, including pain from injection. A seizure immediately post-vaccine would be less likely to be an epileptic seizure, but for those with a confirmed diagnosis then cumulative stress and sleep deprivation could contribute. |
| 7 | **Any other business**<br>• No other business<br>• Meeting closed with karakia. |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 21 July 2021 |
| **Time:** | 3.30-5.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Enver Yousuf, Dr Hilary Longhurst, Dr Tom Hills, Dr Anya Werno, Professor Chris Frampton, Saskia Schuitemaker, Dr Kyle Eggleton, Associate Professor Michael Tatley, s 9(2)(g)(ii) s 9(2)(g)(ii) |
| **Apologies:** | Dr Nick Cutfield, Dr Ian Town, Dr Owen Sinclair, Professor Lisa Stamp, Associate Professor Matt Doogue, Professor Thomas Lumley |
| **Secretariat Support:** | s 9(2)(g)(ii) |

| Item | Notes |
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| 1 | **Karakia and Welcome** |
| 2 | **Minutes of last meeting and update from CVIP Steering Group**<br>• Meeting minutes from 21 June were read:<br>o wording under 4. should be amended to reflect that the frail elderly *could* pass away from the stress relating to a vaccine but it is not necessarily the case.<br>• Mr John Tait provided an update from Steering Group, with the following comments:<br>o The majority of discussion was around myocarditis in young males<br>o CV-TAG had met yesterday to have a deep dive into the topic<br>o The need to consider risk/benefit when giving frail people the vaccine<br>o A case was discussed at the last meeting s 18(c)(ii) |

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| | s 18(c)(ii) [redacted] |
| 3 | **Rapid cycle analysis (RCA)**<br>Presentation from s 9(2)(g)(ii) [redacted], noting:<br>• RCA provides near real time monitoring of AESIs<br>• Background rates drawn from the SAFE study by UoA<br>• RCA presented for anaphylaxis, Bell's Palsy and mortality:<br>  ○ Anaphylaxis: cumulative risk can be found to be elevated compared with what is ordinarily observed.<br>  ○ Bell's palsy: cumulative risk has a wide CI which does not show a statistically significant change compared to background rates.<br>  ○ Mortality: data show that we are currently seeing 70% of the deaths compared to what is normally seen.<br>• Limited by the 2019 background rates which are not reflective of the current context<br>• Comparing passive adverse events with emergency data; mitigated by accessing hospital discharge data flow.<br><br>Discussion:<br>• Where possible, the definitions used for criteria for AESIs (including acquisition, diagnosis or definition) should reflect international definitions (e.g. sourced from JAMA)<br>• Background rate limitations cannot be overcome due to the difference in communicable diseases. These must therefore be taken into consideration when reporting any RCA outcomes. Possible mitigations may require further investigation into background rates in 2020/2021 thus far. |
| 4 | **Overview of AEFI reports**<br>s 9(2)(g)(ii) [redacted] provided an overview of the AEFI reports, noting:<br><br>• A graph was presented showing the proportion of AEFI by ethnic group and reporter type:<br>  ○ Māori and Pasifika have significantly less patient reported AEFIs (data not yet normalised per number of vaccinations; could influence data outcomes).<br>  ○ Injection site pain lower in Māori, while reports of nausea appear higher (possibly significant, visually demonstrated).<br>  ○ Majority of reports from CIR vaccinator.<br>  ○ Reports from CIR vaccinators appeared to be the same across ethnicities with only small differences in what was reported.<br>• **Recommended** that the ability to report is advertised to consumers of the vaccine<br>• Qlik app for hospitalisations was shown. It was noted that it hasn't yet finished undergoing proof of concept and is currently missing context related to age and gender. Once a person is vaccinated (1st or 2nd dose) and enters hospital their data is captured in the app.<br><br>Discussion: |

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| | • Question if we have data, pre-COVID, about rates of reporting, so we can understand how the reporting of COVID AEFIs in different ethnic groups sit in the context of historic reporting rates<br>• Comment that we can't compare data as these are different scenarios. |
| 5 | Reported Cases<br>Dr Michael Tatley gave an overview of reported cases.<br><br>Fatal Reports<br>• Three deaths have occurred in the last month<br>  ○ s 18(c)(ii) [redacted]<br><br>Anaphylaxis<br>• 46 reports to date, 20 of which have met Brighton criteria 1-3 for anaphylaxis.<br>• Only 2 cases met the definition for anaphylaxis this month.<br>• Noted that the number of anaphylaxis cases is decreasing.<br>• Agreed that if the numbers continue to track similarly that there is no need to continue to review in this forum and if there is a spike in this AEFI, ISMB will revisit.<br><br>Other cases of note:<br>• Typically seeing many reports of same AEFIs as seen before.<br>• Question raised as to whether the group wants to continue to review these more commonly reported events or focus instead on unusual or emerging events such as seizures/GBS (which may be associated with other comorbidities).<br>• s 9(2)(a) [redacted]<br><br>Discussion:<br>• It was agreed that it was timely at this juncture (with the Board now having had the chance to review over a period of time the nature of events that have been reported), for the Board's focus to shift more towards reviewing and providing advice on the more unusual AEFIs.<br>• It was further agreed that, ongoing, the Board would simply note the more routine cases observed, unless a potential signal was identified through RCA.<br>• With increasing confidence in the safety, efficacy and delivery of the vaccine, this may also influence what the ISMB reviews. It was highlighted that equitable distribution of the vaccine may also be considered. |

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| | • Question raised as to whether upcoming decisions eg use in under 16 yo, would influence future monitoring decisions from the CVIP, and therefore the focus of the ISMB reviews. For example, reviewing myocarditis in younger people.<br>  ○ s 9(2)(g)(i) [redacted]<br>  ○ The face-to-face meeting in August will provide a good opportunity to discuss the future direction of the Board and talk through some of these issues, along with gaining sight from the CVIP on policy issues needing guidance. |
| 6 | Memos<br>*Thrombosis*<br><br>s 9(2)(g)(ii) [redacted] presented the memo, noting:<br>• Despite most concerns being attributed to other COVID-19 vaccines (e.g. JJJ, AZ), the concern for Comirnaty persists.<br>• 16 thrombotic events have been observed following Comirnaty.<br>• The incidence of thrombosis/thromboembolic events in NZ was also presented<br>  ○ The highest rates are observed in older populations (i.e. 70 plus), with increased risk as age increases.<br>• Two cases in literature were presented with no causal link found<br>• Further comparative analyses show higher rates of thrombo-haemorrhagic events in AZ compared to Comirnaty, with Comirnaty not showing increased rates.<br>• Thrombosis/thromboembolism has not been linked to Comirnaty in any international pharmacovigilance surveillance system.<br><br>Discussion:<br>• It was noted that the incidence of thrombosis has been decreasing over time. Thrombosis captured in hospital events may not accurately reflect the true incidence of thrombosis in the population as a lot is managed in primary care.<br>• Comment as to whether a more accurate denominator could be used to identify the true background rate.<br>• Non thrombocytopenia related data is re-assuring; it was commented that members of the public and healthcare professionals may not be clear on the difference between thrombosis vs. thrombocytopenia related thrombosis >> need to educate the public around how rare the latter is.<br><br>**Action** s 9(2)(g)(ii) [redacted] to put together information for both healthcare professionals and public on the difference between thrombosis and thrombocytopenia related thrombosis.<br><br>*Seizure*<br><br>s 9(2)(g)(ii) [redacted] presented the memo, noting:<br>• 5 cases presented with seizures; s 9(2)(a) [redacted]<br>• International studies reviewed, 2 showed no increase in seizure rate; overall international guidance is that there is no increased risk of seizures.<br>• Seizure not considered to represent a safety signal with the data presented<br>• **Recommended** that Medsafe to monitor through normal pharmacovigilance activities. |

Discussion/comments:

- Comment about the denominators used for observed vs. expected. Most seizures occur in the community and not the hospitals so difficult to compare the data.
- Indicated that access to GP data is possible, however the seizures currently used as background rates must be viewed as a conservative estimate.
- s 9(2)(g)(ii) has reached out to s 9(2)(a) to see if we can get access to GP data for better comparisons (challenging with different PMS providers).
- It was agreed that there is insufficient data to confirm a possible safety signal for seizures and to keep monitoring the issue.

*Adverse events reported by age*

s 9(2)(g)(ii) spoke to the memo, noting:

- There has been significant interest in the media around this
- Reporting rates are lower in older population/Māori
- Number of AEFI per 1000 is trending downwards in the older age group/reporting rates in the passive system lower in the 65+ group, could be due to AEFIs being viewed as "normal" in this age group, a higher threshold for reporting and reduced access to reporting mechanisms.
- Reporting rates can be calculated for individual adverse event terms based on spontaneous reports, but these should be interpreted with caution. The reporting rate is not the same as the incidence rate due to under reporting.
- When compared to reports for people aged 20-29 years, the terms reported for people aged 70 years and over are very similar. The following AEFIs: diarrhoea, herpes zoster, hypertension, malaise, oral paraesthesia, pruritis, tachycardia and tremor were reported in a higher proportion of cases in people over 70 years compared with people aged 20-29 years.
- Compared to people of any ethnicity aged 20-29 years, terms that were reported in a higher proportion of cases in Māori aged 60 years and older, included: chest discomfort, cough, dysgeusia, epistaxis, herpes zoster, hypertension, hypotension, influenza like illness, oedema peripheral, pallor, palpitations, paraesthesia, paraesthesia oral, pruritus, rash erythematous, rash pruritic and wheezing. This needs to be interpreted with caution, due to the small number of reports.
- Fewer report from GPs and pharmacists for Māori aged 60 years or older compared to people aged over 70 years and people aged 20-29 years of any ethnicity.
- CVIP could alert healthcare professionals to under reporting by contacting the relevant professional bodies with a reminder to ask their Māori and other non-European patients about AEFIs.
- Literature appears to agree with the findings of the clinical trial in that local and systemic reactogenicity was seen less commonly in older people. Small study sizes did not lend themselves to comparisons for less common AEFIs.
- Findings from international regulators appear to be reassuring but significance of these AEFIs to the individual should not be dismissed. Some of the reported adverse events may have a significant impact on morbidity in susceptible individuals.
- It is recommended that the New Zealand data sheet for Comirnaty is updated to include the text regarding the need for individual benefit-risk assessments in the frail elderly, as per the Australian product information.

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| | Discussion:<br>• The question was raised as to how many of the aged residential care residents had been vaccinated. s 9(2)(g)(ii) advised that all ARC facilities are now coming to the end of the process.<br>• Comment that in most cases the risk/benefit is in favour of vaccination<br>• It was noted that even if elderly have limited life expectancy, vaccinating can help protect the individual and those around them. Most elderly, who are competent to consent are willing to be vaccinated, and discrimination is not suitable. Given no signal has yet been found that death is a consequence of vaccination, it is important to ensure they have the opportunity to be vaccinated.<br>• CV-TAG have also considered use of the vaccine in the frail elderly; guidance provided and available on the IMAC website.<br>• Risks need to be talked about with the elderly and their families.<br>• It was agreed that it is important to give the public as much information as possible. Therefore, **the Board recommended** adding text around risk/benefit assessment for the frail elderly to the NZ data sheet. |
| 7 | **Update on myocarditis**<br>s 9(2)(g)(ii) *provided an overview of myocarditis in NZ following Cominarty, noting the following:*<br><br>• Data is drawn from from Qlik app.<br>• Not everyone is hospitalised, and background rates relate to those hospitalised.<br>• Number of cases doesn't compare to US. NZ not currently seeing the higher rates, possibly due to current roll out strategy.<br>• A warning has been added to the data sheet for the risk of myocarditis.<br>• A communication has been submitted regarding this adverse event.<br>• Coding issue with Qlik app – can also be pericarditis being reported which may result in over-stating of these events.<br>• May also be stimulated reporting from NZ clinicians due to their awareness of international safety signals.<br>• Background rates in 2020/21 are plausibly lower than previous years due to reduction of respiratory viruses. If we have a lower rate now, this is probably due to truly less myocarditis due to the Border closure.<br>• Health Canada & FDA have rolled out the vaccine to children 12+ years so far, no increase in cases of myocarditis.<br><br>Discussion:<br><br>• Question around how this information informs policy decisions around the roll-out to 12-15 yo. The Director-General is currently receiving advice concurrently from the Regulator, Medsafe and CV-TAG. The D-G then makes recommendations to the Vaccine Ministers for a decision.<br>  ○ It was agreed that the ISMB should also have the opportunity to feed into this process, ie, communicate that they have had the opportunity to review the data and are reassured by what has been seen to date.<br>• Draft guidance from CV-TAG around myocarditis is currently to extend the interval between first and second doses for the under-30s. The Board questioned the data to support this and the effect of the delayed dose on the immunogenic response.<br>• This guidance could impact significantly on the vaccine rollout. |

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| | **Action for** Chair to send a memo to the Chair, CV-TAG to request opportunity for ISMB to see evidence supporting CV-TAG's recommendations on myocarditis. CV-ISMB members to forward any further comments to s 9(2)(g)(ii) who will circulate a draft by Thursday 22nd July. |
| 8 | **AOB – Terms of Reference**<br><br>s 9(2)(g)(ii) advised that the TOR had been updated with suggested changes from the last meeting and circulated with the agenda.<br>**Action for** ISMB members to send any further changes to s 9(2)(g)(ii) by email. A final version will then be circulated for sign off.<br><br>**Stepped AEFI protocol**<br><br>The protocol is a piece of work looking at how to manage a post-event issue and the process to align with internal stakeholders. It was presented for noting in particular regarding the CV-ISMB's role in being brought together for an ad-hoc meeting.<br><br>The next iteration will be brought back to the August meeting.<br><br>**Meeting closed at 5.15pm**<br>**Next meeting: Wednesday 18th August (both face-to face and via VC)** |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 25 August 2021 |
| **Time:** | 4.00 - 5.30 pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Enver Yousuf, Dr Hilary Longhurst, Dr Tom Hills, Professor Chris Frampton, Saskia Schuitemaker, Dr Kyle Eggleton, Dr Nick Cutfield, Dr Maryann Heather, Dr Owen Sinclair, Professor Lisa Stamp, Associate Professor Matt Doogue, Professor Ralph Stewart, Dr Laura Young, Dr Ian Town, Associate Professor Michael Tatley, s 9(2)(g)(ii) s 9(2)(g)(ii) |
| **Apologies:** | Professor Thomas Lumley, Dr Anja Werno |
| **Secretariat Support:** | s 9(2)(g)(ii) |

| Item | Notes |
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| 1 | **Karakia Tīmatanga (Opening prayer)** |
| 2 | **New members and Deputy Chair**<br>• New members welcomed to the group – Ralph Stewart and Laura Young<br>• Announcement of Deputy Chair – Hilary Longhurst |
| 3 | **Meeting minutes**<br>• Minutes from last meeting read and accepted |
| 4 | **Myocarditis update**<br>• Chair advised that memo had been sent to Director-General and National Director CVIP on Friday 13th August following meeting on myocarditis fatal report.<br>• A follow up email was sent on 23rd August indicating myocarditis was the likely cause of death in this individual, however there were other factors s 9(2)(a) s 9(2)(a)<br>• Chair noted the forensic pathologist has concluded that the death was linked to the vaccine. A draft publication has been prepared. |

s 9(2)(g)(ii) *gives an update of the cases of myo/pericarditis reported in NZ for Comirnaty*

- To date, 32 cases of myocarditis, pericarditis and myopericarditis have been reported to CARM.
- Twelve cases are myocarditis (8 female, 4 male); 7 after dose 2 and 5 after dose 1.
- Most cases reported are middle age and older individuals (>40 years); likely due to the sequencing of the vaccination programme rather than a greater risk in these age groups.
- Thirteen cases are pericarditis (6 female, 7 male), 11 after dose 2 and 2 after dose 1. The cases are evenly distributed across the age ranges.
- For myo/pericarditis cases after dose 1: the ages range between 31 to 91 years, with the time to onset generally quite soon after the vaccination event.
- For myo/pericarditis after dose 2: the ages range between 24 to 73 years. The dose interval between dose 1 and dose 2 for cases varies between 21 to 43 days.
- Hospitalisation data (~1 month lag) shows 7 cases of myocarditis after vaccination, we can take confidence from this in the reporting rate to CARM.
- Cases of myopericarditis are assumed to be coded as myocarditis and pericarditis, so there will be some overlap.

s 9(2)(g)(ii) *gives an update of rapid cycle analysis work for myocarditis and mortality*

- Rapid cycle analysis (RCA) for myocarditis, with a monitoring time of 21 days after dose 1 and dose 2, did not identify a statistically significant risk of myocarditis (February-July). When the monitoring time is reduced to 7 days after dose 1, an increased relative risk was observed for June.
- RCA for myocarditis and myopericarditis was further investigated at 21 days after dose 1 and dose 2, with a statistically significant risk observed for June and July. With a monitoring time of 7 days after dose 1, the signal is observed in May, June and July.
- RCA for mortality rates, across 10-year age groups for May, June and July. All age groups have a statistically lower risk of mortality, however 80+ has a slightly elevated risk which is observed across May-July.
- Request for feedback from the Board about inclusion criteria used for the myocarditis analysis, advice on any next steps that Medsafe/the Programme should take and thoughts on publishing mortality rates on the Medsafe website.

Discussion

- Question regarding mortality rates if the observed and expected were switched on the dataset. It was emphasised this outcome would be important to publish. It was further noted that other factors such as comorbidities should also be considered to see if other factors could account for these increased rates.
- It was noted that the vaccine has been given to large number of people in rest homes and/or hospital level care.
- Comment that the deaths in older individuals were likely due to comorbidities rather than the vaccine.
- Regarding the cumulative myocarditis/myopericarditis risk, comment that there was a wide confidence interval which was driving the levels of statistical significance; given the low case numbers, the significance of this was questioned.
- Asked how the background rates were determined, given 2020 had lower circulating viruses, therefore it could be speculated that myocarditis presented at a lower frequency. Answered that the 2019 background rate for myocarditis was used. Noted that multiple years could be used to identify a more robust background rate.

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| | • Comment if it was worth reducing monitoring time to 2 or 3 days for the myocarditis RCA.<br>• Comment that mortality RCA was not unexpected; however, group needs to be cautious as frail elderly were vaccinated, and the deaths may not be unexpected, or necessarily a signal. In these individuals an immune response may have been enough to start a chain of events which could lead to death. Information relayed to the public needs to be careful and considered to ensure no undue distress.<br>• Asked if there was any further information regarding timing of mortality. Answered that the risk window could be adjusted to a shorter time frame to investigate a different outcome.<br>• Noted a reduction in circulating viruses last year had meant that a large number of New Zealanders who were statistically likely to die, did not die, and therefore our mortality last year will always be less than what we are observing this year. Caution was advised when interpreting this data to include the possibility of this bias.<br>• Suggestion that a temporal analysis of time of vaccination and death could be conducted to investigate if there is a peak to investigate a mechanistic association instead of comparing with an overall picture. |
| 5 | **Memos**<br>s 9(2)(g)(ii) *presents information on thrombocytopenia following Comirnaty*<br>• Reports of immune/idiopathic thrombocytopenia purpura (ITP) with other vaccines.<br>• Up to 31st July, CARM have received 5 reports of thrombocytopenia/ITP<br>• Of these cases, 2 cases were considered probable/possibly linked to the vaccine.<br>• The background incidence of thrombocytopenia in NZ is consistent with international figures; highest incidence in the 80+ age group.<br>• Observed rate of thrombocytopenia following vaccination is lower than expected. However, there are limitations, including the possible underestimation of cases.<br>• Pfizer have also evaluated thrombocytopenia and ITP and no safety signals were found based on review of cases or observed verses expected analysis.<br>• From 2 US case-series study reports; 15 cases (up to 4th February) of thrombocytopenia reported following Comirnaty vaccine. The authors could not rule out an association between ITP and mRNA vaccines, however the observed incidence was not greater than the expected rate.<br>• MHRA, EMA and FDA have also not indicated a safety signal.<br>• Overall, there is insufficient information to confirm a safety signal for Comirnaty and thrombocytopenia. It is recommended to continue monitoring via routine pharmacovigilance.<br><br>Discussion<br>• Comment that it is unclear if the background rates of thrombocytopenia is a useful method of detecting incidence across the population given there are multiple causes for thrombocytopenia. Vaccine associated ITP is well described and does occur. Clinical recommendation currently is for chronic ITP patients to receive the vaccine, and their platelets be monitored. s 9(2)(g)(i) [redacted]<br>• Comment that the rate reported through a surveillance system compared to national minimum dataset, which is collected differently, can easily over or underestimate the frequency of the cases. RCA needs to use consistent data collection when looking at current and historic rates.<br>• s 9(2)(g)(i) [redacted]. It was felt that data are reassuring at this stage and that to continue monitoring is the best way forward. |

s 9(2)(g)(ii) *presents information on tinnitus following Comirnaty*

- Up to 10th August CARM have received 61 reported cases, affecting 56 individuals.
- Of these, 31 were female and 25 men, mostly aged 50-69. Forty cases occurred after dose 1 and 34 of the 61 cases are reported as not yet recovered.
- Background rate is unknown. It can be persistent or self-limiting. A UK study found the prevalence of tinnitus to be around 10.1% of the adult population.
- Of the 34 ongoing cases, 18 reports stated a length of time for tinnitus still being present (>8 weeks in 2 reports), with 11 individuals having had tinnitus before.
- s 9(2)(ba)(ii) [redacted]
- Other COVID-19 vaccines, including Janssen and Vaxzevria have also shown link to tinnitus. Janssen has listed tinnitus as an adverse reaction.
- Suggested mechanisms were briefly discussed. These included:
  - a hypersensitivity reaction causing an abnormal autoimmune response
  - vasculitic event
  - dysregulated autoimmune response
  - autoimmune inner ear disease
  - immunisation anxiety-related

Discussion

- Comment that tinnitus commonly presents in the general population. The pathophysiology was mostly idiopathic, and diagnosis can be difficult. The description of tinnitus can vary on presentation and may be observed more frequently in individuals with anxiety due to heightened awareness.
- Comment that the current evidence did not present a concern at this stage.

s 9(2)(g)(ii) *presents information on Guillain-Barré Syndrome (GBS) and COVID-19 vaccines*

- Background rate for GBS in NZ is 2.13 cases per 100,000 persons.
- There has been an increase in number of GBS reports with adenovirus vector COVID-19 vaccines (AstraZeneca and Janssen); both datasheets have been updated.
- No increase in reports for Comirnaty. s 9(2)(ba)(ii) [redacted]
- In addition, the FDA has investigated GBS with mRNA vaccines (Pfizer and Moderna). A crude reporting rate per million doses of vaccine has been found, but no O/E has yet been reported due to the outcomes being insignificant
- Up to 31st July CARM has received three suspected cases, two with sufficient data.
- s 9(2)(a) [redacted]
- Rough O/E analysis with NZ data; the observed rate was less than the expected.

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| | • It was asked if the two cases represent GBS and if the time between vaccination and symptoms are consistent with vaccine induced GBS. Medsafe plan to continue monitoring via routine pharmacovigilance. Asked if there was any additional advice or communication to the public from the Board.<br><br>Discussion<br>• Comment it was not for the Board to decide if these cases represented GBS and this decision should be made by the treating clinician.<br>• Noted that case B was not felt to be convincing or consistent with the clinical patterning of GBS.<br>• Comment for case A, that the time to reaction was too fast to be caused by vaccination. Noted that GBS has often been attributed as a consequence of vaccine administration, but it was cautioned that this probable causation may be historically erroneous.<br>• Comment that more information is required to ascertain the causalities of these presentations.<br>• Dr Michael Tatley noted that there is a limitation when getting valuable or useful data back for these cases.<br><br>s 9(2)(g)(ii) *presents information on Glomerular diseases and Comirnaty*<br>• Features of nephrotic syndrome and nephritic syndrome described.<br>• Background rates of hospitalisations show ~500 cases per year, a lot are diagnosed incidentally.<br>• Hospitalisation data shows that glomerular diseases are quite frequent, but they may not have been part of the CARM investigation.<br>• The spontaneous reports to date for Comirnaty in the renal and urinary disorders system organ class include urinary tract infections, haematuria (may be related to other disease), kidney injury and 3 cases of nephrotic syndrome.<br>• Cases don't present a clear pattern, it was observed there were more cases for dose 1, but time to onset varied (<1 to 17 days).<br>• Bomback et al referenced, this review investigated cases of kidney disease in the literature which are linked with the COVID-19 vaccines. Mostly observed to be related to Moderna vaccine but can also be associated with Pfizer vaccine. If it is true, it is likely related to mRNA vaccines as opposed to other vaccine platforms.<br>• The EMA has recently decided that this was a signal for mRNA vaccines and have begun their assessment. Their conclusions will be available in a couple of weeks.<br>• Medsafe propose to continue monitoring and request a copy of review from Pfizer. Asked if the Board considered other actions or communications were needed.<br><br>Discussion<br>• Comment that there was no particular concern at this stage, and support was provided for Medsafe's suggested actions. |
| 6 | **Reported cases**<br>*Dr Michael Tatley provides an overview of reported cases*<br><br><u>Fatal reports</u><br>• There had been an increased number of fatal reports in the last month.<br>• Each report is followed up where needed to obtain further information.<br>• Cases are up until 1 week prior to the postponed meeting (18 August).<br>  ○ s 18(c)(ii) [redacted] |

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| | ○ s 18(c)(ii) [redacted]<br>• Some of these cases overall are felt to be related to a comorbidity, and other cases are unclear on what the link could be.<br><br>Discussion<br>• Comment regarding case 9: Forensic pathologist contacted a member of the Board to discuss this case. s 18(c)(ii) [redacted]<br>• s 9(2)(g)(i) [redacted]<br><br><u>Other cases of note</u><br>• Summary provided of cases of thrombocytopenia.<br>• Suspected case of s 9(2)(a) [redacted] |
| 7 | **AOB**<br><u>Myocarditis fatal report</u><br>• s 9(2)(g)(ii) [redacted] noted the Director-General and National Director CVIP wanted to thank the Board for the work that went into the meeting and memo.<br>• An update was provided yesterday to the Vaccine Minister's meeting chaired by the Prime Minister.<br>• Public announcement is accepted in the coming days; a press release is being prepared.<br><br><u>Expense claims</u> |

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| | • Continuity lost due to change in personnel, all expense claims moving forward to be sent to CVIP Business support<br>• **Action** for s 9(2)(g)(ii) to send an email to the Board detailing updated process<br><br><u>Active Monitoring</u><br>• Post Vaccination Symptom Check (PVSC) will begin this week<br>• It will look to have a coverage of 10% of the vaccinated population, with oversampling for Māori and Pacific peoples to improve equitable understanding of reactions in these populations.<br>• Further detail to be provided at the next meeting. |
| 8 | **Karakia whakamutunga (closing prayer)** |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 15 September 2021 |
| **Time:** | 4.00-6.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Members:** | Dr Enver Yousuf, Associate Professor Matt Doogue, Dr Hilary Longhurst, Dr Tom Hills, Dr Maryann Heather, Professor Chris Frampton, Saskia Schuitemaker, Dr Kyle Eggleton, Dr Nick Cutfield, Professor Thomas Lumley, Dr Owen Sinclair, Professor Lisa Stamp, Professor Ralph Stewart, Dr Laura Young, Dr Anja Werno, Associate Professor Michael Tatley |
| **Ministry of Health Attendees:** | s 9(2)(g)(ii) [redacted] |
| **Guests:** | s 9(2)(g)(ii) [redacted] |
| **Apologies:** | Dr Ian Town |
| **Secretariat Support:** | s 9(2)(g)(ii) [redacted] |

| Item | Notes |
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| 1 | **Karakia and Welcome**<br>• Minutes from 25 August meeting accepted. |
| 2 | **Reporting to date**<br>s 9(2)(g)(ii) [redacted] *provides an overview of the reporting to date. Specifically notes the underreporting in Pasifika.*<br>• It was noted that the IIAG looks at how the programme is implementing the rollout with an equity lens. It was asked for a view regarding what more the programme needs to do to help assist Pacific peoples.<br>• Comment that Pacific peoples do under report. The main issues are a delay in reporting and unclarity around what to report.<br>• s 9(2)(g)(i) [redacted]<br>• Answered by Dr Tatley from the perspective of CARM that whilst it is important to report on everything, it can overwhelm the system. To guide reporters: Serious clinical events should be reported, or ongoing events which do not resolve, or an event which is felt to be clinically unusual. |

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| | • Noted that other cohorts likely to have issue with reporting due to the technology involved. It was further noted, Whakarongorua can also help submit a report and it is necessary to communicate that function to the public better.<br>• It was commented that the reporting rate for Māori was similar to non-Māori; however, it could be age related. The equivalent trend of reporting is a source for comfort, and the trend is improving, but there is more that needs to be done. It was felt if reporting was emphasised for Pacific people, it will enable better reporting for all groups. No recommendations were made at this stage.<br>• Proposed that a communication could be made to the public via a media statement, that Pacific peoples are not reporting and providing simple guidance to the public may help to resolve this. Asked if this can be translated to enable better access.<br>• It was asked if the MoH can enable a media release or press statement. It was answered that the MoH can only act on the recommendations of the CV-ISMB. It was further noted that data from individuals with disability would be appropriate to include as well.<br>• Comment that there is general anxiety in the public after the reporting of the myocarditis case. It was further commented that there is a concern of the nocebo effect. Noted that regardless of the nocebo effect it is important to pick up on AEFIs. |
| 3 | **Fatal Reports and Cases of Note**<br>*Dr Michael Tatley begins by giving an overview on the fatal report of the* s 18(c)(ii) [redacted]<br>• s 18(c)(ii) [redacted]<br>• s 18(c)(ii) [redacted] |

s 18(c)(ii) [redacted]

*Dr Tatley gives a brief overview of other reports of death of note.*

- Noted that it is necessary for members of the CV-ISMB to have a look independently at the cases and decide if there is anything that requires discussion.
- In most instances individuals with significant comorbidities or advancing age.

*Dr Tatley presents the case of a* s 9(2)(a) *who died post vaccination.*

- s 18(c)(ii) [redacted]

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| | s 18(c)(ii) [redacted] |
| | *Case of* s 9(2)(a) *was discussed.*<br>• s 18(c)(ii) [redacted]<br>• Noted that the CV-ISMB can issue guidance to forensic pathologists to include investigation of myocarditis during PM.<br>• Comment that CV-ISMB could issue some guidance around PM investigations, directed towards ICU clinicians and cardiologists.<br>• Asked if the communication could be adjusted to tell people what the Board does and what information/investigations are needed to support discussions by the Board around the role of the vaccine in a particular adverse event. |

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| | • Noted that the Board might need a regular communication out to the sector and/or public. Comment that this would need to be discussed and currently not within Board's remit.<br>• Dr Tatley noted that it can be a struggle to find further information from hospitals and GPs. Therefore, establishing a quicker route is essential.<br>ACTION: Memo to be sent to CVIP National Director establishing that in instances of sudden cardiac death, CV-ISMB recommends cardiac histopathology to discount death due to myocarditis.<br><br>*Other cases of note referenced*<br>• s 9(2)(a) [redacted]<br>• Myocarditis and pericarditis<br>• Herpes zoster reactivations<br>• Nephrotic syndrome<br>• Vasovagal reaction leading to subdural injury |
| 4 | **Memo on AEFIs in children and adolescents**<br>s 9(2)(g)(ii) [redacted] *gives an overview of Comirnaty and AEFIs in children and adolescents.*<br>• Vaccination in 12–15-year-olds started 3 weeks ago; AEFI reports in 12–19-year-olds is 3.3 per 1000 doses given.<br>• Reported symptoms like what has been observed in adults, with expected reactions. Some of the common symptoms could also be associated with anxiety receiving the vaccine itself, (e.g., dizziness, nausea and vomiting).<br>• Asked what a serious event in a child is classified as. Answered that serious events are classified when the event results in death, is life threatening, results in persisting disability, hospitalisation, congenital abnormality or is medically significant.<br>• Noted that chest pains may be due to a stress response or can be due to many other circumstances besides myocarditis.<br>• Asked if there was establishment of myocarditis as a diagnosis in a specific case, but it was answered that the ECG was inconclusive, and troponin was only mildly elevated. The paediatrician presented the possibility of myocarditis, but this was not advanced beyond that point. |
| 5 | **Update on Support to the Pacific**<br>s 9(2)(g)(ii) [redacted] *gives an overview of pharmacovigilance support to the Pacific. It is noted that this function is provided through the Global Health directorate and priority is given to the Realm.*<br>• The Realm (Cook Islands, Niue and Tokelau) have completed their respective roll outs in adult population; all have requested Pfizer vaccines for their 12–15-year-olds (to be sent in September).<br>• Comment that people should be congratulated on this significant effort. |
| 6 | **Myocarditis update** |

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| | s 9(2)(g)(ii) *provides an overview of the cases of myocarditis and overview of the proposed mechanism by which this adverse event may occur.*<br>• It was noted that we had 60 cases as of 9 September 2021<br>• 46 had a diagnosis of likely/reasonable myocarditis<br>• As of 15 September 2021, it was noted that we have 84 cases still requiring investigation.<br>• Of the 84 cases; 18 are between 12-29 years old (three under 18 years old) and 10 cases were after the second dose.<br>• Time to onset is generally one-two days after vaccination event; however, this has been reported to be significantly longer in some cases.<br>• Paper by Bozkurt et al. was discussed in regard to proposed mechanisms of myocarditis with mRNA COVID-19 vaccines; paper requested to be added to CV-ISMB Teams channel. |
| 7 | **AOB**<br>• Following the recommendation of the CV-ISMB around communications at the 9 August meeting; a desktop review has been conducted regarding communications around myocarditis to sector and public.<br>ACTION: s 9(2)(g)(ii) will email summary of this to CV-ISMB members |
| 8 | **Karakia and Close** |

# Minutes

# Independent Safety Monitoring Board

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| **Date:** | 6 October 2021 |
| **Time:** | 4.00-6.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Enver Yousuf, Associate Professor Matt Doogue, Dr Hilary Longhurst, Dr Tom Hills, Professor Chris Frampton, Saskia Schuitemaker, Dr Kyle Eggleton, Dr Nick Cutfield, Professor Thomas Lumley, Dr Owen Sinclair, Professor Lisa Stamp, Professor Ralph Stewart, Dr Anja Werno, Associate Professor Michael Tatley |
| **Ministry of Health Attendees:** | s 9(2)(g)(ii) [redacted] |
| **Guests:** | s 9(2)(g)(ii) [redacted] |
| **Apologies:** | Dr Ian Town, Dr Maryann Heather, Dr Laura Young |
| **Secretariat Support:** | s 9(2)(g)(ii) [redacted] |

| Item | Notes |
|---|---|
| 1 | **Karakia and Welcome**<br>• Minutes from 15 September meeting accepted. |
| 2 | **Communications safety messaging**<br>*The Chair,* s 9(2)(g)(ii) [redacted] *provide an overview of how the work of the CV-ISMB could be used to strengthen public confidence in the vaccine's safety.*<br>• The Chair noted that a report on function, processes and evaluations of the CV-ISMB would be beneficial. Agreed that this messaging will need to include investigations into safety signals and safety concerns.<br>• Communications noted that a report is important to emphasise the findings of the Board (i.e., that the Pfizer-BioNTech vaccine is safe).<br>• From a communications perspective three areas of focus could be:<br>  ○ generation of report<br>  ○ formal press release, including an interview component to provide an overview of all members<br>  ○ video content with Board members, possibly in a webinar style<br>• The goal is to provide the story of how pharmacovigilance and safety monitoring works. Needs to be provided in a format that is readable by people from all age groups and levels of science knowledge. |

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| | • Ministry noted there is a lot of misinformation circulating in media, and supported the improved transparency with the public, specifically regarding the findings of the CV-ISMB<br>• Comment around whether any content produced could be translated into Māori and Pacific languages to support equity.<br>• Consumer representative emphasised that she has been advocating for some time for more engagement with the public by the CV-ISMB to provide information about its functions and findings.<br>• Ministry noted that the public is particularly interested in independent voices that keep the Ministry accountable.<br>• Noted that this represents an opportunity to provide more dialogue for this concerned about vaccine safety or hesitant to vaccination due to safety concerns.<br>• Noted that at the root of misinformation is a lack of trust of authority, and this collaboration would be central to dissipating that.<br>• Comment that research into barriers to vaccination has showed that across all cohorts the largest concerns were around long-term side effects, the speed of development of the vaccine and underlying health conditions.<br>• Noted that in a report for the CV-ISMB it would be necessary to highlight that not all reported adverse events are seen by the Board.<br>• Consideration should be given to where report sits, as if available on Ministry website, may not be seen as independent.<br>• Agreement from the Board for a repot to be written and structure to be agreed on via email. |
| 3 | **Update on the COVID-19 Vaccine & Immunisation Programme (CVIP)**<br>s 9(2)(g)(ii) *provides an overview of the changes happening within the CVIP.*<br>• As of today, we have reached 50% of eligible population fully vaccinated and 80% have had first dose and 82% have at least a booking.<br>• There is a 90% goal set by the government, but this is outside of the Programme's scope. The purpose of the CVIP was to provide eligible individuals the opportunity to be vaccinate<br>• Noted that the programme ends in December, however there are a lot of variables as we move to future state: individuals who will age into the programme, those who want a different vaccine platform and the question of booster doses. Still a lot of work for the programme and this may look different in the future, however safety assurance remains a priority and work of the CV-ISMB must remain ongoing.<br>• Chair to confirm with the Director General and National Director CVIP the ongoing need for the CV-ISMB into Q1.<br>• Noted that a pathway to normalisation for a business-as-usual function is essential for the CV-ISMB.<br>• Question around whether this will have an impact on the communications strategy previously discussed, and if this is then better done as the CVIP rather than the CV-ISMB. Answered that there is an opportunity here for the Board to mark a line between what it did for the CVIP and what it can do going forward. |

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| | • CARM highlighted that what needs to be avoided is what happened in the early 2000s with the Meningococcal vaccination programme. Where many insights were gained but ultimately lost after the programme dissolved. It is now essential those same mistakes are not repeated.<br>• A consensus around these points was felt. |
| 4 | **Update on Rapid Cycle Analysis**<br>s 9(2)(g)(ii) *provides an update on the on-going rapid cycle analysis work*<br>• Safety concern had previously been identified for death rates in the 80+ age group after the second dose.<br>• A survival analysis corrected for age across 10-year age bands found in the 80–90-year-olds there was no increased risk in mortality between those vaccinated and not vaccinated.<br>• Individuals partially vaccinated did present a signal, but this was thought to be due to underlying conditions which prevent further vaccination. The analysis was repeated for 90+ year olds, with no signal found.<br>• Question, if the Board was satisfied with the data analysis done on the death rates for the 80+ age group and the conclusion that there is not a safety signal.<br>• CV-ISMB provided thanks for this work to date and considered to be useful and insightful.<br>• CARM echoed this and requested whether the UoA could be consulted and perhaps present their work from the SAFE study to the Board to see if they have similar outcomes. |
| 5 | **Thrombosis update**<br>s 9(2)(g)(ii) *provides an update to the July review of thrombosis as a potential safety signal.*<br>• There is no more international evidence<br>• Up until 28 September; 107 reports of thrombotic events to CARM (45 cases of DVT, 30 case of PE, 15 case of DVT and PE and rest were other thrombotic events).<br>• Investigated by other regulatory agencies; MHRA, EMA, FDA and TGA have not identified thrombosis and thromboembolic events as a safety signal for the Pfizer-BioNTech vaccine.<br>• Number of internal studies have not found a link; three papers have demonstrated a possible causal link which therefore requires further monitoring.<br>• Discussion around Hippisley-Cox (2021) et al. paper which disagrees with other studies to date; comments around methodologies used and requires further critical review.<br>• Medsafe to continue monitoring through routine pharmacovigilance activities. An update on stroke will be provided at an upcoming CV-ISMB |
| 7 | **Fatal Reports and Cases of Note**<br>*Michael Tatley begins by giving an overview on the fatal reports to date.*<br>• s 18(c)(ii) [redacted] |

s 18(c)(ii)

- [redacted]
- CARM concluded by encouraging the Board to review the list of cases pending investigation discussed in the meeting and follow up directly with CARM if it's considered that further information should be sought for a specific case.

*Michael Tatley gives an overview of non-fatal reports of note received since the last meeting.*

- s 9(2)(a)
  - [redacted]

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| | • s 9(2)(a) [redacted]<br>• Noted that the Epilepsy Organisation in the US has noted that in some instances after vaccination the resulting fever may lower the seizure threshold, however, a safety signal has not yet been identified from this.<br>• The Chair thanked CARM for their efforts in this work. |
| 8 | **Any other business**<br>• Chair advised that there is a request to add Fiji to the Terms of Reference as a country from the Pacific which the Board might be asked to provide advice.<br>• Draft ToR with proposed addition in Teams channel. |
| 9 | **Karakia and close** |

# Minutes

MINISTRY OF HEALTH
MANATŪ HAUORA

# Independent Safety Monitoring Board

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| **Date:** | 27 October 2021 |
| **Time:** | 4.00-6.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Members:** | Dr Enver Yousuf, Associate Professor Matt Doogue, Dr Hilary Longhurst, Dr Maryann Heather, Professor Chris Frampton, Saskia Schuitemaker, Dr Nick Cutfield, Professor Thomas Lumley, Dr Owen Sinclair, Professor Ralph Stewart, Dr Laura Young, Dr Anja Werno, Associate Professor Michael Tatley, Dr Susan Kenyon, s 9(2)(g)(ii) [redacted] |
| **Ministry of Health Attendees:** | s 9(2)(g)(ii) [redacted] |
| **Apologies:** | Dr Ian Town, Dr Tom Hills, Dr Kyle Eggleton, Professor Lisa Stamp |
| **Secretariat Support:** | s 9(2)(g)(ii) [redacted], |

| Item | Notes |
|---|---|
| 1 | **Karakia and Welcome**<br>• Minutes from 06 October meeting accepted. |
| 2 | **Updates from the Chair**<br>*John Tait provides an update to the Board about recent actions out of the CV-ISMB and recent discussions from CV-TAG*<br>• Noted that the National Director of the COVID-19 Vaccine and Immunisation Programme (CVIP) has agreed to communications being sent to pathologists to consider cardio histology in cases of sudden cardiac death following vaccination and to the wider health sector to consider post-mortems for sudden deaths that have occurred in close temporal proximity to a vaccination.<br>• The communications are being prepared by the Post-Event team and will be circulated to the CV-ISMB for review early next week.<br>• Noted that the Director General has agreed to the necessity of the CV-ISMB, and the Board will continue in its role for at least the first quarter of 2022. |

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| | • CV-ISMB was invited to discuss myocarditis at recent CV-TAG meeting and the cardiologist on the CV-ISMB was thanked for his excellent contribution to this.<br>• Noted that CV-TAG has concerns around underreporting of cases of myocarditis, as a result, CV-ISMB noted to CV-TAG that comparison of hospitalisation data and reported cases shows similar numbers; CV-TAG remain concerned about mild cases not being reported.<br>• Noted that IMAC has a list of individuals not recommended for a second dose.<br>• Noted that CV-TAG is considering Pfizer vaccinations for those aged 5-11 years and booster doses for the eligible population. |
| 3 | **Update on the CVIP**<br>s 9(2)(g)(ii) *provides an overview of the changes happening within the CVIP.*<br>• As of today, we have reached 71% of eligible population fully vaccinated and 87% have had first dose.<br>• It was highlighted that the goal remains achieving 90% vaccine uptake and that the Programme's focus is completely on capturing that last 3%, therefore. As bookings appear to have begun to drop off, it seems that the last 3% will be hard to capture.<br>• Medsafe is considering the Pfizer vaccine for those aged 5-11 years.<br>• The need for a second vaccine is evident, there will hopefully be some announcement of this soon; both Janssen and AstraZeneca are approved by Medsafe and hope to have AstraZeneca available end of November.<br>• Noted that concomitant vaccinations have been approved and this has now been implemented by the Programme.<br>• It was lastly noted that the Director General has signed a letter of comfort assuring that the Programme will continue into 2022 and therefore there will be secretariat support for the CV-ISMB from within the CVIP. |
| 4 | **Post Vaccine Symptom Check Overview**<br>s 9(2)(g)(ii) *provided an overview on Post Vaccine Symptom Check (PVSC), its purpose and its current functionality.*<br>• It was asked how participants are recruited, with particular concern for the proper recruitment of Māori and Pasifika participants.<br>• Answered that both Māori and Pasifika have always been oversampled by the PVSC system, previously 20% of participants recruited were Māori and 14% Pasifika, but recently it has been decided to oversample even further and therefore now 30% of participants will be Māori and 20% Pasifika. |
| 5 | **Menstrual disorder and Pregnancy memos**<br>s 9(2)(g)(ii) *provides an overview of the reporting of menstrual disorders to date and the investigation on the possible link to the Pfizer COVID-19 vaccine.*<br>• Commented that parameters such as heavy or light are extremely subjective, making it difficult to identify if there is a significant change.<br>• Noted that the most convincing data is that from clinical trials, where there is a control group.<br>• It was agreed and further noted that when the question is about an increase in rate of common disorders the RCA data is therefore necessary. |

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| | • Comment that there is merit to providing communications to the public to provide reassurance that menstrual disorders are not a serious adverse event and could be occurring for various reasons.<br>• It was further commented that these communications should be combined with any communications about pregnancy and fertility.<br>• There was a strong agreement to this from CV-ISMB members.<br>• It was noted that in primary care there is a significant number of questions around pregnancy, menstrual bleeding, and fertility after COVID-19 vaccination.<br>• s 9(2)(g)(i) [redacted]<br>s 9(2)(g)(ii) [redacted] *gives an overview of the literature around safety of the vaccine for pregnant woman and an update of cases reported to date.*<br>• It was commented that there is a lot of concerning data emerging out of the UK about COVID-19 in pregnant unvaccinated woman with the Delta variant, with many cases of stillbirths as a result. In contrast there is no effect from the vaccine on fertility, miscarriage, and congenital abnormalities.<br>• There was agreement to this point from other CV-ISMB members.<br>• Asked if there was national data about the rate of congenital abnormalities.<br>• It was answered by Medsafe that including Tongue-tie (ankyloglossia), the rate is 7% and this includes minor abnormalities.<br>• It was also noted that when doing data comparisons, it is critical we understand the time points at which these happen, as many teratogenic things can occur during weeks 1 to 12 of gestation and very few are vaccinated during this time.<br>• Comment that communications around this must also go out to the public, including the fact that the CV-ISMB has reviewed the data around safety for pregnant woman and has concluded that the vaccine is safe for them.<br>• There was a strong agreement to this from CV-ISMB members.<br>• Medsafe agreed that there are not safety concerns for pregnancy but there are significant concerns for stillbirths as a result of COVID-19 infection.<br>• It was noted that providing information around stillbirths in other countries is therefore necessary.<br>• It was further commented that this is an instance where the risk of negative health outcomes for pregnant woman because of COVID-19 infection is high and the risk of vaccination is minimal so the messaging around this needs to be strong.<br>• There was agreement to this from CV-ISMB members.<br>• Commented that the Maternity team within the Ministry is putting out information, so it is worth Post Event liaising with them for this purpose.<br>ACTION: Communications will be created around the COVID-19 vaccine and menstrual bleeding, fertility, and pregnancy. |
| 6 | **Myocarditis Update** |

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| | s 9(2)(g)(ii) s 9(2)(g)(ii) *gives an update on myocarditis reporting to date.* s 9(2)(g)(ii) *and provide an overview about the myocarditis follow-up study to be conducted by Medsafe and Post Event.*<br>• The CV-ISMB commented that the risk of myocarditis is observed mostly in young men, but this is not what it seen by New Zealand data.<br>• Answered that New Zealand represents a small sample size so there may not be enough people to observe such a trend with.<br>• It was further added that we may not have vaccinated enough young people for that particular trend to be visible.<br>• It was asked if we have the NHIs of each patient to do in depth investigations into the markers of myocarditis and medications and comorbidities present in those who presented with it.<br>• Answered that the healthcare professional surveys in the study will seek to answer those questions.<br>• It was asked what the purpose of the study is, and it was noted that the rational for the study is unclear.<br>• Answered by Medsafe that the long-term consequences of cases of myocarditis is unknown, but it was also noted that no long-term consequences are expected.<br>• Noted that a research question like that needs proper research oversight and the resources are strained already in terms of pharmacovigilance capacity.<br>• It was further noted that there are reservations amongst the CV-ISMB about the collection of data that is not part of a standard clinical process and not covered by an approved research programme.<br>• The Ministry highlighted that any proposed study will undergo ethical approval and will return to the CV-ISMB for review.<br>• Medsafe highlighted that no one is inquiring into this specific question and that they are mindful that it must be done correctly.<br>• It was noted that CV-TAG has an interest in research into myocarditis and asked if this has been presented at CV-TAG.<br>• It was commented that myocarditis research will be discussed at the next CV-TAG and an update about this project would be beneficial to CV-TAG as well. |
| 7 | **Fatal Reports and Cases of Note**<br>*Michael Tatley begins by giving an overview on the fatal reports to date.*<br>• CARM noted that this is an overview of cases that are needing further insight.<br>• s 18(c)(ii) [redacted]<br>• s 9(2)(a) [redacted] s 18(c)(ii) [redacted] |

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| | s 18(c)(ii) [redacted]<br>• It was acknowledged that this explanation eased any concerns.<br>• It was agreed that CARM's comments are factual, and it was noted that there is no cluster of these cases, which would be reason for concern.<br>• s 18(c)(ii) [redacted]<br>• Comment that it is not our role to get involved in individual cases unless it is a specific comment for the forensic pathologist.<br>• There was agreement to this point, but it was acknowledged that the CV-ISMB must look at deaths that implicate the vaccine to determine if there is a reason to believe the vaccine could be linked.<br>*Michael Tatley gives on overview of non-fatal reports of note.*<br>• s 9(2)(a) [redacted]<br>• Comment that it is unclear why possible long COVID is suggested and that there is limited understanding of how to diagnose and treat long COVID.<br>• s 9(2)(a) [redacted]<br>• Noted that confirming there is no signal for aseptic meningitis may be necessary.<br>• s 9(2)(a) [redacted]<br>• It was further noted that it is unlikely the vaccine has a role in congenital abnormalities as if that was the case, we would expect to see an increase in cases of spontaneous abortions. |
| 8 | **AOB**<br>• An email was sent out requesting profiles from CV-ISMB members, that have yet to provide these. Profiles will be incorporated into annual report.<br>• It was highlighted that MedSafety week is from the 1st of November to the 7th of November and communications by Medsafe will be out on twitter, it was noted that members can retweet the communications if they wish to. |
| 9 | **Karakia and Close** |

# Minutes

MINISTRY OF HEALTH
MANATŪ HAUORA

# Independent Safety Monitoring Board

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| **Date:** | 17 November 2021 |
| **Time:** | 4.00-6.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Members:** | Dr Enver Yousuf, Dr Hilary Longhurst, Dr Maryann Heather, Saskia Schuitemaker, Dr Nick Cutfield, Professor Thomas Lumley, Dr Owen Sinclair, Professor Ralph Stewart, Dr Anja Werno, Dr Kyle Eggleton, Dr Tom Hills, Professor Chris Frampton, Associate Professor Matt Doogue, Professor Lisa Stamp, Dr Laura Young, Associate Professor Michael Tatley |
| **Ministry of Health Attendees:** | s 9(2)(g)(ii) [redacted] |
| **Guests** | s 9(2)(g)(ii), s 9(2)(a) [redacted] |
| **Apologies:** | Dr Ian Town |
| **Secretariat Support:** | s 9(2)(g)(ii) [redacted] |

| Item | Notes |
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| 1. | **Welcome** |
| 2. | **Minutes from last meeting**<br>• Minutes from last meeting (27 October) accepted. |
| 3. | **Update from CVIP Strategic Communications Team**<br>s 9(2)(g)(ii) [redacted] *provided an update of current work going on in the COVID-19 Vaccine and Immunisation Programme strategic communications space.*<br>• Communications around COVID-19 vaccination in pregnancy is a focus, with communications going out to both the health sector and the public. Key messaging that the vaccine is safe in pregnancy and the possible consequences of COVID-19 infection are much worse.<br>• A pamphlet on pregnancy has been distributed to DHBs and the most recent sector newsletter included a piece on vaccination during pregnancy. The sector newsletter goes out to 22,000 subscribers, including vaccinators, other health care professionals and members of the public.<br>• A Facebook live session Q&A session relating to vaccination in pregnancy was recently held with an expert panel. |

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| | • Medsafe Monitoring communications on menstrual disorders and vaccine safety in pregnancy are now published.<br>• Vaccine hesitancy remains an issue during pregnancy, mainly due to safety concerns for the foetus, and this came out of the Facebook live Q&A session.<br>• s 9(2)(g)(i) [redacted]<br>• There will be an opportunity for Board members to have input into upcoming communications, including future Facebook live Q&A sessions relating to vaccine safety, and other targeted communications relating to the vaccine persona and vaccine hesitancy.<br>• The Board raised concern that targeted communications focusing on the persona of an unvaccinated individual may deter Māori from engaging with health services, as it puts the blame at an individual level rather than focusing on systemic issues that have contributed to lower vaccination rates amongst Māori.<br>• Responded that this will be fed back to the wider Strategic Communications team.<br>• It was asked to what extent the Strategic Communications team liaise with the Immunisation Advisory Centre (IMAC) regarding communications.<br>• It was answered that they work closely with IMAC to assure messages align and to share content for sector updates. |
| 4. | **Update on the SAFE study**<br>s 9(2)(a) [redacted] *provided an update on background rates of adverse events of special interest from the SAFE study and current safety activities within the Global Vaccine Data Network including rapid cycle analysis.*<br>• Discussion about the possible use of association studies which use a modified case-control design where cases also act as their own controls.<br>• Discussion about the unique position of New Zealand to conduct association studies due to having minimal circulating COVID-19 infection – particularly relevant for myocarditis as COVID-19 infection can itself cause myocarditis.<br>• The Board asked for clarification on how CVIP and Medsafe conduct rapid cycle analysis (RCA).<br>• CVIP explained that rapid cycle analysis allows for early detection of possible safety signals and utilises background rate data from the SAFE study. |
| 5. | **Update on the CVIP**<br>s 9(2)(g)(ii) [redacted] *provided an overview of the current key focuses within the CVIP.*<br>• A priority is to continue driving vaccine uptake across the country, with a focus on equity (Māori, Pasifika, and disability). This will involve ongoing engagement with DHBs, Crown and local partners, and public communication campaigns.<br>• Other key focuses include the move to the COVID-19 Protection Framework (traffic light system), vaccine certificates, vaccine mandates and exemptions, boosters, AstraZeneca vaccine, and vaccination of 5-11-year-olds.<br>• Vaccine certificates (available from 17 November 2021) and technology to allow businesses to verify vaccine certificates will be key to the COVID-19 Protection Framework. |

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| | • Booster doses and the AstraZeneca as an alternate vaccine will be available from the end of November (bookings to open on 26 November 2021).<br>• It was noted that up to 400,000+ people may be eligible for boosters before the end of 2021.<br>• Vaccinations in 5-11-year-old's have not yet been approved by Medsafe.<br>• The CVIP will seek technical advice from the COVID-19 Technical Advisory Group (CV-TAG) as part of the planning process relating to implementation of vaccinations in 5-11-year-olds.<br>• It was asked whether AstraZeneca will be available to anyone, or if it's use will be restricted.<br>• Answered that it will be available to anyone 18 years and over who cannot receive the Pfizer vaccine, or who would like a different option other than the Pfizer vaccine. |
| 6. | **Stroke and Erythema Multiforme Memos**<br>s 9(2)(g)(ii) *provided an overview of cases of stroke reported following Pfizer COVID-19 vaccination in New Zealand to date and the investigation into a possible link to the vaccine.*<br>• It was noted that this topic was previously presented to the CV-ISMB in June 2021, and the recommendation at that time was for Medsafe to continue monitoring this issue.<br>• It was noted that a case involving a traumatic subdural haemorrhage s 9(2)(a) was included in the analysis.<br>• The Board commented that traumatic subdural haemorrhage is not typically considered a stroke and that this type of case could be removed from the analysis.<br>• The Board agreed that current evidence does not suggest a safety signal for stroke, and that Medsafe should continue to monitor this issue.<br><br>ACTION: Medsafe to remove case of traumatic subdural haemorrhage from the analysis.<br><br>s 9(2)(g)(ii) *provided an overview of cases of erythema multiforme reported following Pfizer COVID-19 vaccination in New Zealand to date and the investigation into a possible link to the vaccine.*<br>• Aetiology of erythema multiforme was discussed.<br>• It was commented that erythema multiforme is typically a clinical diagnosis, and that misclassification can occur.<br>• It was also noted that it is not uncommon in normal clinical practice for a precipitating cause to not be identified.<br>• Asked whether erythema multiforme was reported in the Pfizer clinical trials.<br>• Medsafe/CVIP responded that they will look into this and report back to the Board with the answer.<br>• The Board agreed that current evidence does not suggest a safety signal for erythema multiforme, and that Medsafe should continue to monitor this issue.<br><br>ACTION: Medsafe/CVIP to report back to CV-ISMB with Pfizer clinical trial data on erythema multiforme. |

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| 7. | **Myocarditis and Pericarditis Follow-up Update**<br>s 9(2)(g)(ii) *provided an update on the progress of the planned study on long-term outcomes in people who have experienced myocarditis and/or pericarditis after COVID-19 vaccination in New Zealand.*<br>• It was noted that a Research Oversight Committee is being established to provide study governance, and that ethics approval will be sought, with the aim of commencing participant recruitment in early 2022. |
| 8. | **Fatal Reports and Cases of Note**<br>*Michael Tatley provided an overview of the recent fatal reports.*<br>• It was noted that there can be a lag in reporting, with some cases of death not reported to CARM until weeks after the death occurred.<br>• Five cases currently under investigation were discussed, which included s 18(c)(ii) [redacted]<br>• It was noted that further information on these cases is still pending and will be brought back to the Board for discussion when more information is received.<br>• s 18(c)(ii) [redacted]<br>• Question from Board about if myocarditis was considered in this case.<br>• Answered that final report from forensic pathologist is still pending.<br>• s 18(c)(ii) [redacted]<br>• Answered that it is unclear if this was done in this case, but final report from forensic pathologist is still pending.<br>• s 18(c)(ii) [redacted] |

s 18(c)(ii) [redacted].

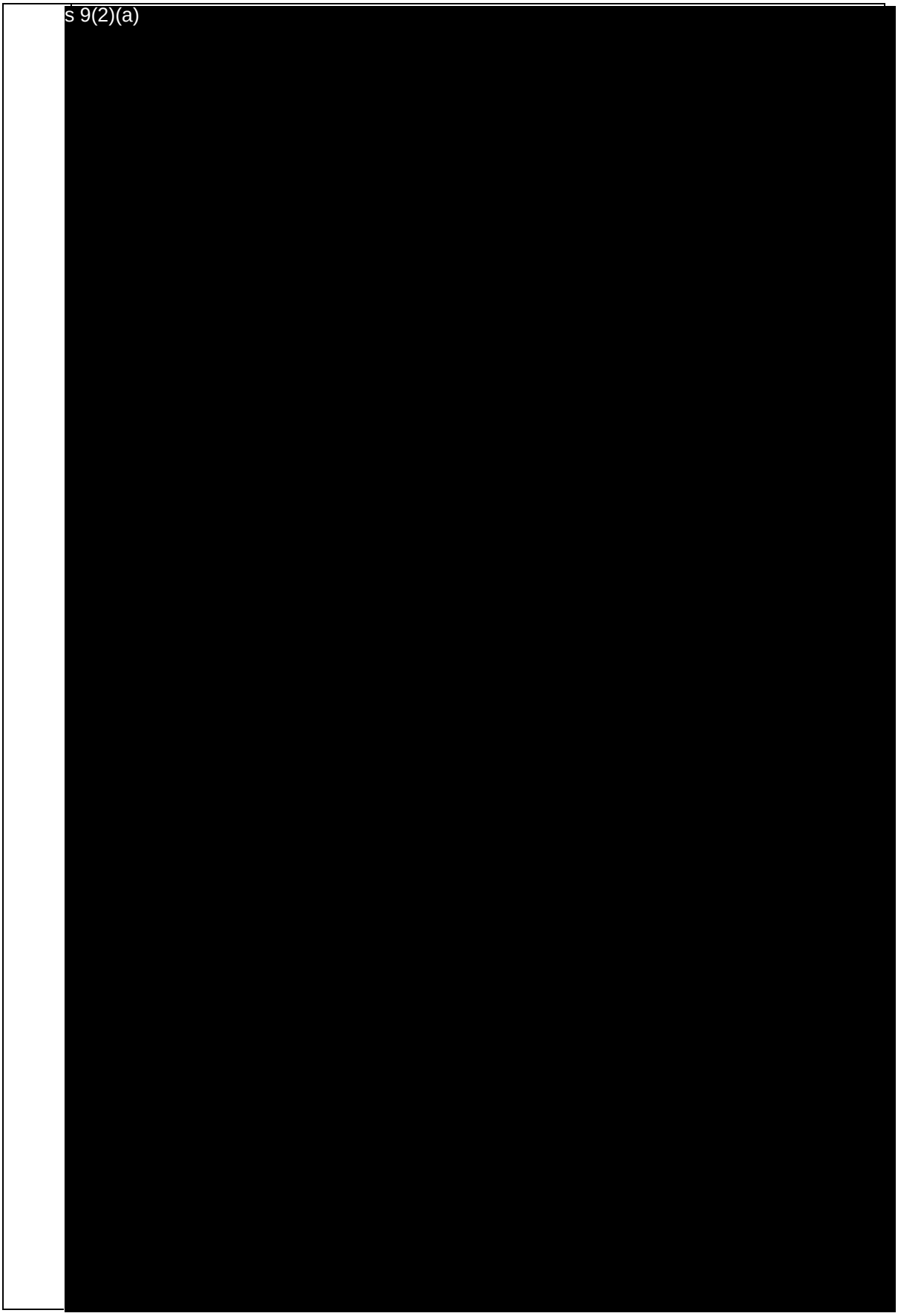
- It was noted that there was interest from Ministers and the DG for a view from the CV-ISMB on this case.
- s 18(c)(ii) [redacted]
- The CV-ISMB restated their previous recommendation that a post-mortem and histology be considered in any deaths where myocarditis is considered a possible cause.
- Other fatal cases discussed which CARM consider unlikely related to the vaccine, include cases where the deaths appeared to be due to worsening of underlying cardiac, respiratory, and renal comorbidities.

ACTION: CARM to make a statement, that cause of death in this case s 9(2)(a) [redacted] s 9(2)(a) [redacted] is unclear, and there is no clear evidence that the death is due to myocarditis.

*Michael Tatley provided on overview of the recent non-fatal reports of note.*

- s 9(2)(a) [redacted]

s 9(2)(a)



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| | s 9(2)(a) [redacted] |
| 8 | • The next CV-ISMB meeting on 8 December 2021 will be the last scheduled meeting for the year, with the next scheduled meeting in January 2022. |
| 9 | **Karakia and Close** |

Minutes

# CV-ISMB 15 December 2021 Meeting

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| **Date:** | 15 December 2021 |
| **Time:** | 4.00-6.00pm |
| **Location:** | 133 Molesworth Street, Wellington & Microsoft Teams |
| **Chair:** | Mr John Tait |
| **Attendees:** | Dr Enver Yousuf, Dr Hilary Longhurst, Dr Maryann Heather, Saskia Schuitemaker, Dr Nick Cutfield, Professor Thomas Lumley, Dr Owen Sinclair, Professor Ralph Stewart, Dr Ian Town, Dr Kyle Eggleton, Dr Tom Hills, Professor Lisa Stamp, Dr Laura Young, Associate Professor Michael Tatley |
| **Ministry of Health Attendees:** | s 9(2)(g)(ii) [redacted] |
| **Apologies:** | Dr Anja Werno, Associate Professor Matt Doogue, Professor Chris Frampton |
| **Secretariat Support:** | s 9(2)(g)(ii) [redacted] |

| Item | Notes |
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| 1. | **Welcome and Karakia**<br>• Meeting opened at 4:07 by the Deputy Chair<br>• Karakia performed<br>• Chair arrived shortly after |
| 2. | **Minutes from last meeting**<br>• Minutes from last meeting 17 November accepted. |
| 3. | **Update on Extraordinary Meeting (8 December)**<br>*The Chair provided an update of the Extraordinary Meeting which occurred on the 8th of December.*<br>• The Coroner would like it emphasised that the CV-ISMB does not determine the cause of death and only gives an indication of the probability that the vaccine was involved in the events that led to the death.<br>• An extraordinary meeting is to be organised next year with the Board concerning the s 9(2)(a) [redacted] case once more information is available.<br>• The Chair noted the CV-ISMB statement is being edited before it is published on the website. |
| 4. | **Overview of Reported AEFI for COVID-19 Vaccines**<br>*Medsafe provided an update on AEFI reporting to date including AstraZeneca.* |

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| | • Discussion around the fact that there have been over ten times the usual level of reporting in a year in 2021.<br>• There have been 95 reports so far relating to the AstraZeneca vaccine.<br>• Discussion about the most common reported adverse events and the demographics of these reports. It was noted that females were more likely to report adverse events than males.<br>• Discussion around who is submitting reports, noting that the public, vaccinators, and nurses are the top three groups reporting adverse events.<br>• Discussion around the three top AESIs reported, herpes zoster, pericarditis, and myocarditis.<br>• The ongoing disparity in reporting rates for Pacific peoples compared to other ethnic groups was noted.<br>• A question was asked around what the Ministry is doing to around the underreporting of AEFI in Pacific peoples.<br>• The response was that the Ministry has been working with the Pacific team and Communications within the Ministry to create a two-pronged approach through a public information campaign and information distributed to healthcare professionals through the Pacific chapter of the College of GPs.<br>• It was asked what the use is of encouraging reporting for adverse events that are common and have no treatment.<br>• Another member of the board responded that representative reporting would assist in identifying safety signals that may differ across demographics.<br>• Medsafe noted that high levels of reporting can help with communication to the public about safety and agreed with the previous comment regarding representative reporting. |
| 5. | **Improving COVID-19 Vaccine Uptake**<br>*The Ministry provided an update on analysis of data which were performed to try and examine ways to improve vaccine update.*<br>• Overview of the active and passive safety monitoring systems, the number of vaccine doses administered, and the number of AEFI reports received in New Zealand to date.<br>• Discussion around the correlation between AEFI reporting and second dose hesitancy, including the analysis of people who had the same reaction to dose one and dose two of the Pfizer vaccine.<br>• Outline provided of current initiative of writing letters to people who have had one dose and expressed hesitancy towards a subsequent dose.<br>• A member of the Board commented on prior Medsafe work around the nocebo effect and whether this could be incorporated into vaccine communications.<br>• A member of the Board commented that only a small proportion of the population are still unvaccinated.<br>• A member of the Board asked whether in the analysis of people experiencing adverse events after both doses, the denominator included people who hadn't had the second dose.<br>• The Ministry responded that the denominator included all people who have had dose 1, but that they would check the analysis and respond outside of this meeting. |

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| | • CARM stated that in their experience, responding to the reporter provides a level of reassurance to consumers who have concerns about their events and this is generally done as part of CARM's business as usual processes. However, due to the volume of COVID-19 vaccine reports, individual responses have not been possible.<br>• A member of the Board commented that the adverse event rate may be very high, but most are minor adverse events, related both to the immune response and possibly some nocebo events, and this may be the message that needs to be conveyed to the general public, especially since these events generally resolve on their own in a reasonable period of time.<br>• A member of the Board commented that although individual responses are not possible, general reassurance can be provided to the public and that the pharmacovigilance system existing provides confidence in the vaccine programme.<br>• A member of the Board commented that the nocebo response is often aggravated by detailed listing of adverse effects. In countering the somatic adverse events that often arise from nocebo other strategies are required. Some examples include discussing the nocebo or gaining consent about not describing adverse events in detail. |
| 6. | **AEFIs in Children (12-15) and Herpes Zoster Memos**<br>*The Ministry provided an overview of cases of in children.*<br>• It was noted that the most commonly reported events in the 12-19 age group were consistent with events reported in older age groups.<br>• The percentage of serious adverse events reported for the 12-19 age group was slightly lower than the rate of serious adverse events reported for older age groups.<br>• It was noted that there have been eight reports of myocarditis in the 12-14 age group (five validated) and 13 reports in the 15-19 age group (ten validated)<br>• There was a discussion of the four reported deaths in the 12-19 age group and it was noted that two were found to be unrelated, and one to be suicide. The fourth report is currently still under investigation and was reviewed by the Board at a meeting held on the 8th December.<br>• Myocarditis data from international regulatory authorities was discussed.<br>• The post-marketing safety reports by Pfizer was discussed, post-marketing experience form Pfizer indicates similar rates of adverse events in this age group and no safety signals.<br>• It was concluded that reports of AEFIs in children and adolescents in New Zealand mirrors post-marketing reports from other countries, and that serious cases and deaths would continue to be closely monitored and brought to the attention of the Board.<br>• No questions or comments from the Board.<br><br>ACTION:<br>• Continue to monitor closely through routine pharmacovigilance activities.<br><br>*The Ministry provided an overview of Herpes Zoster following Corminarty vaccination* |

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| | • This is an update to the last time herpes zoster was discussed by the Board, in June.<br>• It was noted that there were 22 reports of herpes zoster, up from seven cases in June.<br>• There was a discussion of herpes zoster cases in people under 20 years of age, as there has been ten reports. It was noted that herpes zoster is most common in older adults but does occur in children and adolescents.<br>• An analysis of observed versus expected for hospitalisation data did not show a raised risk of herpes zoster in any age group.<br>• It was noted that an Israeli study had noted a weak association between the Pfizer vaccine and herpes zoster.<br>• In September 2021, Pfizer provided a special review of herpes zoster in their monthly safety report and concluded there was no safety concern.<br>• No questions or comments from the Board.<br><br>ACTION:<br>• Continue to monitor through routine pharmacovigilance activities. |
| 7. | **Fatal Reports and Cases of Note**<br>*CARM provided an overview of the recent fatal reports.*<br>• s 18(c)(ii) [redacted] |

- s 18(c)(ii) [redacted]
- There were no further questions or comments.

*CARM provided an overview of the recent non-fatal reports of note.*

- The patterns of reporting concerning myo/pericarditis, thrombocytopenia, vasculitis (mostly chilblain-type presentations), spontaneous abortion, pancreatitis, diabetes and hyperglycaemia were discussed.
- Retinal vein occlusions highlighted by CARM as unusual events:
  - s 9(2)(a) [redacted]

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| | • s 9(2)(a) [redacted]<br>• There were no further questions or comments. |
| 8 | **AOB**<br>• The annual draft of the CV-ISMB report was currently being reviewed and that the meeting from the 8th December as well as this meeting on the 15th would be added to the report. |

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| | • The Ministry commented that there was likely to be another extraordinary meeting around the case of s 18(c)(ii) in a s 9(2)(a) in the new year.<br>• The Ministry mentioned that the Post Event team is working through the Christmas break and there is the chance that an extraordinary meeting may be called if an important case was reported during this period.<br>• A member asked about the AstraZeneca vaccine and the role of the CV-ISMB around the risks of AstraZeneca.<br>• Medsafe commented that there is a warning around thrombosis and thrombocytopenia syndrome (TTS) in the data sheet but requested the information around treatment that had been decided in Australia.<br>• It was commented by a member of the Board that Australia has a broader range of possible treatment plans available than New Zealand and that trans-Tasman cooperation may be required if a case occurred. It was noted that Australia has very clear guidelines on testing and what to do when VITT is expected and that it may be appropriate for us to follow those – these are going to be circulated amongst medical professionals. Key is early treatment, so HCPs need to know what to do if a possible case occurs. This may involve sending samples to Australia to be tested.<br>• It was noted that only 2672 people had received the AstraZeneca vaccine in New Zealand to date.<br>• The Chair acknowledged the work of the board over 2021. |
| 9 | **Karakia and Closing**<br>• Meeting concluded at 5:40pm with a Karakia. |