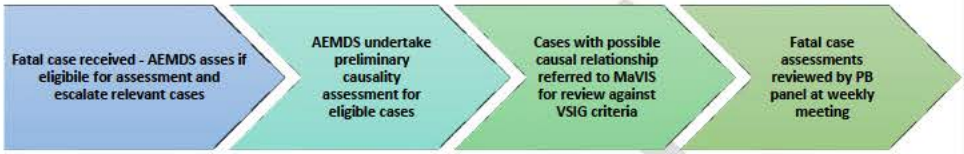
Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

OFFICE USE ONLY

AEMDS Preliminary Assessment of COVID-19 vaccine Fatal Case

Process Overview

Purpose of this process is for AEMDS to identify cases with a possible causal relationship that require consideration by MaVIS against VSIG criteria. It is not a formal causality assessment.



Case Details

AEMS CASE NUMBER & LINK	
PATIENT AGE, SEX & STATE	
COVID-19 VACCINE	*[COVID-19 vaccine tradename]*
DATE OF AEMS REPORT	*[date report was created in AEMS]*
DATE OF ASSESSMENT	*[date this form is completed]*

Commented [S22]: NOTE TO REVIEWERS
PLEASE REMOVE all comment blurbs (including this one!) and ALL PURPLE TEXT from the complete form before attaching it to the case in AEMS.

Step 1: Eligibility for Assessment

Step 1: Eligibility for Assessment *For a case to be eligible, ALL of the following minimum criteria need to be met:*			
		YES	**NO**
Q1	**Does the report identify the vaccine that was administered?**	☐	☐
Q2	**Is there confirmation that the vaccine was administered before the event?** (i e., vaccination date and AEFI data available in the AEMS report, and in temporal association order) *For reports of 'disease recurrence/flare/aggravation', did the reported change in pre-existing disease occur after the vaccination date?*	☐	☐
Q3	**Does the report identify an Adverse event* which had a fatal outcome?** **The reported AE could be an unfavourable or unintended sign, an abnormal laboratory finding, a symptom or a disease. A report of only "death" without any information on what caused the death (fatal AE/AEFI) entered as valid case in AEMS, but it would be considered ineligible for assessment pending further information*	☐	☐
	ELIGIBLE FOR ASSESSMENT?	☐	☐

If YES:	If NO, case is NOT eligible for assessment:
• **ATTACH this assessment form to the case in AEMS after filling in *'Case details'* & *'Step 1'* and *'Step 3'*** (Refer to 'Naming Convention' section below)	• **End Assessment and request further information from the reporter.** • **ATTACH this assessment form to the case in AEMS after filling in *'Case details'* & *'Step 1'* and *'Step 3'*.**

Reference/Publication #

• **ACCEPT** the case in AEMS with a decision type of ***'Causality: possible'*** • **PROCEED** to ***'Step 2: Preliminary Causality Assessment'*** (OR **Assign** completed case to senior AEMDS EL1 for performing Step 2)	• **ACCEPT** the case in AEMS with a decision type of ***'Causality: possible'*** • ***Referral to MaVIS: NOT required*** • ***Escalation to PB AS & MO5: MAY BE required (as FYI only)*** *(Refer to' Guidance for Referral and Escalation on Page 3)* ↓ **Proceed** to ***'Step 3: Recommendation'***

Further Information Requested?	**YES** ☐	**NO** ☐

Details and Rationale: *Briefly document the rationale for requesting/not requesting further info, and details of information requested.*

Step 2: Preliminary Assessment of Causality

This step is performed by a senior AEMDS EL1, who will fill out the table below in the form created and attached to the AEMS case at Step 1.

Step 2: Preliminary Causality Assessment ***Does the information suggest a possible causal link between vaccination and cause of death?***			
Q1	**Is the reported AEFI/Cause of death expected with this vaccine?** **Assessed against current PI.*	Y/N and briefly explain	
Q2	**In this patient, did a specific test demonstrate the causal role of the vaccine?**	Y/N and briefly explain	
Q4	**Is there an obvious non-vaccine cause reported?** *In this patient, does the medical history, clinical diagnosis or underlying medical condition, suggest another cause for the event?*	Y/N and briefly explain	
Causal link between vaccination and reported fatal AEFI? # ↓ **PROCEED to *'Step 3: Recommendation'***		**POSSIBLE** ☐	**UNLIKELY** ☐

Reviewer Comments: *Describe any additional/ambiguous/uncertain aspects of causality assessment not completely covered by the questions above.*

*# Regardless of this Preliminary Assessment of Causality, **ALL Fatal AEFI** cases will **always** be assigned as **"Causality: Possible" within AEMS** to ensure the case is included in our data analytics.*

Step 3: Recommendation

Step 3: Recommendation for Referral to MAVIS/Escalation to PB AS & MO5 ***Does the case meet the criteria for Referral to MAVIS for further evaluation AND/OR Escalation to PB AS & MO5?***		
Is the case Eligible for Assessment?	**YES** ☐	**NO** ☐
REFER to MaVIS for assessment against VSIG criteria?	**YES** ☐	**NO** ☐
ESCALATE to PB AS & PBPMA *(For information or to COVID-19 PV meeting?)*	**YES** ☐	**NO** ☐

Rationale for Recommendation: *Describe briefly. Refer to the 'Guidance for Referral and Escalation'*

Recommendation reviewed and endorsed at meeting with PMA: *Include meeting date*

Guidance for Referral and Escalation

Referral to MaVIS AND/OR Escalate to PB AS & MO5			
STEP 1	**Is the case eligible for assessment?**	**NO**	→ **REFERRAL to MaVIS for assessment is NOT required** *(Document and request key missing information from reporter)* • If Age<18 years AND/OR fatal Myocarditis/TTS → **ESCALATE to PB AS & MO5 (As FYI only)**
		YES	- Case is **assessable**, proceed to **Step 2** *(Send to Senior AEMDS EL1 for Prelim Causality Assessment)*
STEP 2	**Preliminary Causality Assessment**	**Unlikely**	• If Age >18 years AND Non-AESI (Not Myocarditis/TTS) → **REFERRAL to MaVIS for assessment NOT required** *(This is subject to case-by-case assessment. Document rationale and discuss at Weekly Fatal Case Meeting)* • If Age<18 years AND/OR fatal Myocarditis/TTS → **REFER to MaVIS for assessment AND ESCALATE to PB AS & MO5**
		Possible	• If Case has **sufficient information** to allow meaningful MaVIS assessment against VSIG criteria • **REFER to MaVIS for assessment against VSIG criteria** • Where causality is possible, but AEMDS consider the **information in the cases is insufficient** for meaningful MaVIS assessment against VSIG criteria then: • **DO NOT Refer to MaVIS for assessment against VSIG criteria** • If Age<18 years AND/OR fatal Myocarditis/TTS • **REFER to MaVIS for assessment AND ESCALATE to PB AS & PBPMA** • If Causality is possible and the AEFI expected/listed AEFI (included in PI) • **REFER to MaVIS for assessment AND ESCALATE to PB AS & PBPMA** *(to be discussed at COVID-19 PV meetings)*

Commented S22: Usually these would be cases where a causal link cannot be excluded due to temporal association, but there is insufficient information:
- To meaningfully assess causality any further
- For MaVIS to assess the case against VSIG criteria

For eg: death following vaccination, but coroner's reporter not available or inconclusive.

While these cases may not be referred to MaVIS individually, they form art of pool for signal detection and will be assessed qualitatively as part of signal investigation activities.

Commented S22: Escalation to PBMA for further action, including communication.

Naming Convention

- The assessment form for the initial version of a fatal COVID Vaccine Case in AEMS should be named in the following format, before attaching to the case in AEMS:

'AEMDS Fatal ICSR Preliminary Assessment Form - AU-TGA-0000XXXXXX – YYYYMMDD - Initial'

The YYYYMMDD date is for the date the form is completed.

- The assessment form for a follow up/amendment version of a fatal COVID Vaccine Case in AEMS should be named in the following format:

'AEMDS Fatal ICSR Preliminary Assessment Form - AU-TGA-0000XXXXXX – YYYYMMDD - Amendment'

An AEMDS Preliminary assessment may not be required for every subsequent version of a fatal ICSR. The AEMDS reviewer should assess whether the follow up information received for a case requires a fresh assessment, based on whether the new information can potentially affect the initial assessment decisions, i.e, causality assessment, referral to MaVIS and/or escalation to PB AS & MO5.

Background

The reporting of an adverse event or death following vaccination to the Therapeutic Goods Administration (TGA) does not mean that the vaccine caused these events. The TGA uses information about the reported cause of death (as determined by the treating health professional, hospital or coroner) to look for potential conditions or adverse effects which may be linked to vaccination.

All deaths reported to the TGA in people who have been recently vaccinated against COVID-19 are assessed by TGA staff to determine whether the information provided suggests a possible link between vaccination and the causes of death, or if further information is required to make an assessment. These case reviews follow a standardised assessment process based on WHO guidelines to consider the strength of the evidence available to determine whether the clinical conditions which led to a fatal outcome represent an emerging (new) safety signal for the vaccine.

When another cause for the events that resulted in death is not medically obvious, not stated and cannot be determined from the initial report, the TGA requests further information from the reporter (which may include the results of investigations relating to the death or past medical history, post-mortem examination findings, the death certificate, and results of a Coronial Office investigation) and undertakes further assessment of the case based on the WHO guidelines.

Adverse event reports with a fatal outcome remain in the TGA database and coded as "causality possible" even if they have not been assessed as vaccine related. This approach ensures that all reports are included in analyses to detect safety signals based on patterns of reporting.

The TGA provides the total number of adverse event reports with fatal outcome, and the number assessed as vaccine related, in its weekly COVID-19 vaccine safety report.

AEFI Causality Assessment

Causality assessment of an adverse event following immunisation (AEFI) is the systematic review of data to arrive at a conclusion that the evidence is either consistent with the vaccine being a cause, is inconsistent with the vaccine being a cause, or is indeterminate.

The Therapeutic Goods Administration (TGA) uses the World Health Organisation (WHO) causality assessment framework, www.who.int/publications/i/item/9789241516990, to guide the structure and considerations of causality assessment. Criteria which are assessed in this process include:

- whether there is a temporal relationship between the vaccine and the event
- biological plausibility
- population-based evidence for causality
- definitive proof that the vaccine caused the event, and
- consideration of alternative explanations.

Vaccine Investigation Safety Group (VSIG)

The TGA refers fatal cases (or groups of cases) that may have an impact on the overall benefit-risk balance or threaten public confidence to the vaccine to a Vaccine Safety Investigation Group, which is a panel of independent medical and vaccine experts.

Importantly, the VSIG should only be used in accordance with the above criteria. This is aligned with international guidelines from the World Health Organisation. As stated in the WHO guidance, it is important avoid burning out the panel by taking cases that don't meet criteria, or taking cases before we have document essential to the process like finalised autopsy reports or outstanding investigations. The VSIG is NOT a case review panel, should not adjudicate unclear cases, is not designed to re-confirm the patient's diagnosis and is NOT required for the COVID-19 vaccine claims scheme.

Of note, the VSIG criteria are as follows:

Commented [S22 [redacted]]: should we add what VSIG does not do (i e. it is not the referral point for cases that TGA can't determine causality for)

1) When an **AEFI of concern** or a **safety signal of concern** is identified by the TGA or OHP (office of health protection); AND
2) The TGA and OHP agree that the AEFI or signal:
    a. Has the potential to change the favourable benefit-risk balance of the vaccine in a National or State Immunisation program OR
    b. Could threaten public confidence in vaccine safety; AND
3) The case(s) is/are considered **eligible** for assessment and/or investigation.

An **AEFI of concern** is a single serious AEFI that is unexpected and without an obvious non-vaccine cause.

What this assessment does not do

The Therapeutic Goods Administration (TGA) review of fatal cases:

1. Will not confirm, investigate, diagnose or determine the cause of death for an individual:
    a. Medical practitioners and Coroner's in each jurisdiction are responsible for death investigation, assessment and confirmation of cause of death. This is a legal process that is not undertaken by the TGA. The TGA uses information about the reported cause of death (as determined by the treating health professional, hospital or coroner) to look for potential conditions or adverse effects which may be linked to vaccination.
2. Will not re-diagnose the condition suffered by the patient in question or advise on medical care.
3. Will not impact on COVID-19 vaccine compensation applications or influence the assessment of such cases:
    a. The COVID-19 Vaccine Claims Scheme is an independent scheme that focuses on a treating doctor's opinion only. This is separate to the pharmacovigilance processes undertaken by the TGA (such as this case review process) which aims to identify emerging safety signals for a product.
4. The Department of Health accepts that the claims approved via the claims scheme will not necessarily reflect the TGA's case numbers for that condition due to:
    a. The difference between a surveillance case definition and a clinical diagnosis for an individual
    b. Non-mandatory adverse event reporting to the TGA
    c. No requirement for an adverse event report to be submitted to the TGA for a claim to be approved

The review of reports of death is just one aspect of the TGA's close monitoring of the safety of COVID-19 vaccines. The TGA uses a range of different information sources to monitor the safety of vaccines, including reviewing and analysing adverse events report data, working with international regulators, and reviewing medical literature, media and other potential sources of new safety information.