National Pharmaceutical Regulatory Agency
Ministry of Health, Malaysia

Summary Report on Adverse Events Following Immunisation of COVID-19 Vaccines in Malaysia

(Data as of 31st December 2021)[1,2,3]

#2

Introduction

It is almost two years since the start of the COVID-19 pandemic that had claimed over 31,559 lives across the country, to date.[1] The COVID-19 vaccines have been proven to be highly effective in preventing severe illnesses and deaths from COVID-19 infection.[4-5] In an effort to stall the spread of the infection and end the pandemic, a mass vaccination roll-out was initiated on 24th February 2021 under the **National Immunisation Program for COVID-19 (PICK)** in Malaysia.

Similar to any medicines, vaccines may cause side-effects commonly known as adverse event following immunisation (AEFIs). An AEFI is defined as ***any untoward medical occurrence that follows the administration of a vaccine and may not necessarily be causally related to the vaccine itself.***[6]

Hence, it is inaccurate to assume that all AEFIs reported in this summary report are directly caused by the vaccine.

When millions of vaccines are administered in a short period of time, it is expected to see a surge in the number of adverse events being reported including serious ones. However, reviews of these individual reports often reveal that vaccine does not play a role in the vast majority of these events.

Apart from the vaccines being the cause, the reported adverse events can also occur due to ***fear of injections or the immunisation process, previously undiagnosed illness, underlying diseases, or medications being taken concurrently by the vaccine recipients. These events may also be coincidental that happen to occur shortly after a vaccine was administered.***

How NPRA collects adverse event reports?

Similar to other regulatory agencies, NPRA monitors drugs and vaccines safety through passive surveillance. AEFI reports are collected via the existing **NPRA Adverse Drug Reaction (ADR)/AEFI Reporting System.**

In addition to the current reporting system, during PICK, **notifications of documented minor AEFIs** are also collected from the vaccine recipients through the **MySejahtera Application** in their smartphones

NPRA receives all medicines adverse event reports including AEFIs from pharmaceutical companies, healthcare professionals in government and private health institutions as well as consumers in Malaysia.

*Documented AEFI are **known** adverse events that already described in the product leaflet and are based on global safety data from clinical trials and/or post-marketing safety monitoring.*

NPRA has issued the Malaysian ADR/AEFI Reporting Manual for Healthcare Providers to guide reporters on how to report adverse events.[6] NPRA also continuously highlights the importance of ADR/AEFI reporting and how to report them through periodic communications, several trainings, and awareness campaigns.

*Reports help to identity **signals** that **alert** scientists of possible cause- and-effect relationships that **need to be investigated.***

How NPRA processes AEFI reports and monitors safety of COVID-19 vaccines?

As with any medicine and vaccine, NPRA closely monitors the safety of COVID-19 vaccines. Every adverse event report received at the national centre is carefully processed and assessed by trained pharmacists. When clinically important information is missing from a report, utmost efforts will be made to obtain detailed information.

NPRA requires healthcare providers to report all suspected AEFIs including any death after COVID-19 vaccination, **even if it is unclear whether the vaccine was the cause**. AEFIs are initially categorised into **serious** and **non-serious**. **Serious** AEFIs include those that require hospitalisation, prolong hospitalisation, are life-threatening, or suspected to cause death**. While these events can happen after vaccination, they are rarely caused by the vaccine.** Serious AEFIs are investigated thoroughly by the healthcare facility involved. The investigation report will then be reviewed by the committee of experts, the **Pharmacovigilance Committee of COVID-19 Vaccines (JFK)** to determine if the events are causally linked to the vaccine.

All reports will be subsequently presented to the **Malaysian Adverse Drug Reactions Advisory Committee (MADRAC)** before they are submitted to the **World Health Organisation (WHO) global database**.

Reports recorded in the databases are constantly reviewed and monitored to identify unexpected adverse events or potential safety **signal** for further evaluation. In addition to monitoring local AEFI reports, NPRA also collaborate with Product Registration Holders to monitor and detect any emerging safety issues. NPRA also network with other regulatory agencies to keep abreast with new safety concerns raised globally. This allows rapid detection and assessment of all available safety information on the vaccines to ensure the overall benefit–risk profile of the vaccines remains positive. Any emerging risks of the vaccines will communicated promptly to healthcare professionals and the public as needed.

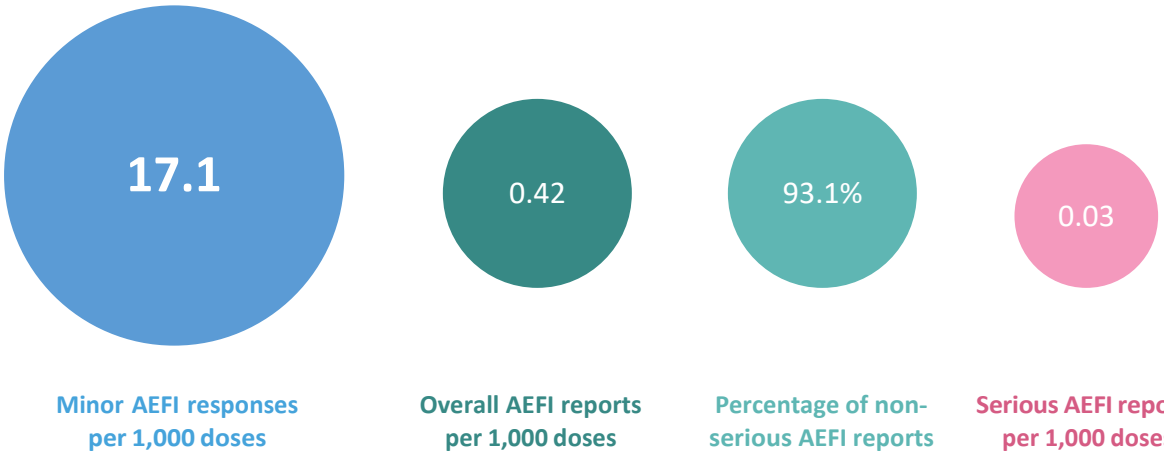
Total Doses of COVID-19 Vaccines Administered[1,2]

Five (5) COVID-19 vaccines are currently in use in Malaysia – Comirnaty (Pfizer-BioNTech), CoronaVac (Sinovac), AstraZeneca, Convidecia (Cansino) and Covilo (Sinopharm). These vaccines have met NPRA's high standards for quality, safety and efficacy. As of 31st December 2021, a total of 57,119,777 COVID-19 vaccine doses have been administered.

Figure 1: Total COVID-19 vaccine doses administered by brand

Comirnaty (Pfizer-BioNtech)	32,120,991 doses
CoronaVac (Sinovac)	20,608,643 doses
AstraZeneca	4,157,338 doses
Convidecia (Cansino)	199,676 doses
Covilo (Sinopharm)	33,129 doses

Rate of Reported Adverse Events[2-3]



AEFI responses received via MySejahtera Application

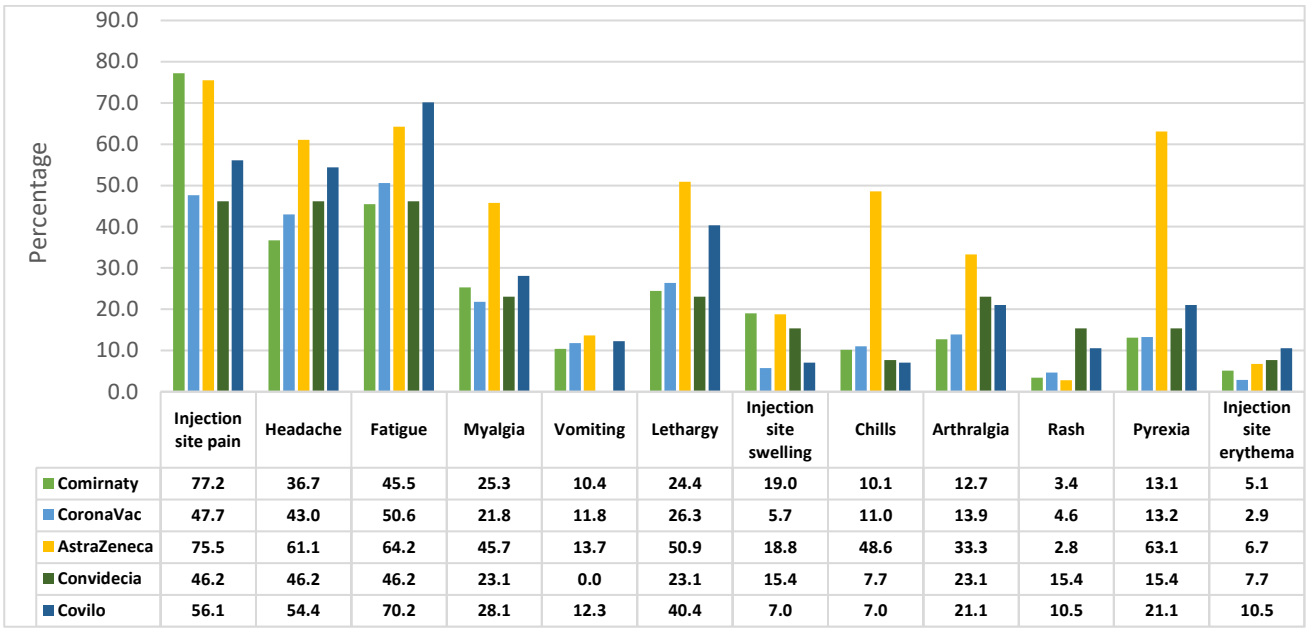
From the start of the vaccine roll-out up to 31st December 2021, the total of minor AEFIs recorded via the MySejahtera Application is 974,134 which is equivalent to 17.1 responses* for every 1,000 doses of vaccines administered.

The most common side effects notified were consistent with those typically observed following vaccination. These include injection site pain, headache, fatigue, muscle or joint pain, lethargy and fever, which will usually recover in a few days with or without treatment.

The reporting trend of these common side-effects were also consistent throughout the monitoring period.

*Important note: *The total number of responses collected may not accurately represent the total number of individuals who experience an adverse event, as every individual may report more than one response.*

Figure 2: Most commonly reported AEFI in MySejahtera Application



	Injection site pain	Headache	Fatigue	Myalgia	Vomiting	Lethargy	Injection site swelling	Chills	Arthralgia	Rash	Pyrexia	Injection site erythema
Comirnaty	77.2	36.7	45.5	25.3	10.4	24.4	19.0	10.1	12.7	3.4	13.1	5.1
CoronaVac	47.7	43.0	50.6	21.8	11.8	26.3	5.7	11.0	13.9	4.6	13.2	2.9
AstraZeneca	75.5	61.1	64.2	45.7	13.7	50.9	18.8	48.6	33.3	2.8	63.1	6.7
Convidecia	46.2	46.2	46.2	23.1	0.0	23.1	15.4	7.7	23.1	15.4	15.4	7.7
Covilo	56.1	54.4	70.2	28.1	12.3	40.4	7.0	7.0	21.1	10.5	21.1	10.5

AEFI reports received via NPRA Reporting System

While through the existing NPRA Reporting System, the total of AEFI reports received was 24,042 which is equivalent to **0.42 reports per 1,000 doses** administered. The majority of reports received, at **93.1% were non-serious**, short-term, and do not pose any potential risk to the health of the vaccine recipients.

Serious adverse events after COVID-19 vaccination occurred but very rarely. During this monitoring period, only 1,652 or 6.9% of the total AEFI reports received were categorised as **serious AEFIs.** Note that the **ACTUAL proportion of serious AEFIs could be much smaller**, as the relatively high number of minor AEFI responses received via the MySejahtera Application should be accounted for in the background. **The reporting rate of serious AEFIs was recorded at 0.03 per 1,000 doses.**

Table 1: Serious AEFI Reports by brand

	Comirnaty	CoronaVac	AstraZeneca	Convidecia	Covilo	Cumulative
Total dose	32,120,991	20,608,643	4,157,338	199,676	33,129	**57,119,777**
Serious AEFI Report	975	540	134	3	0	**1,652**
Serious AEFI / Total AEFI Report (%)	5.4	11.0	11.6	6.7	0	**6.9**
Serious Reporting Rate per 1,000 doses	0.03	0.03	0.03	0.02	0.00	**0.03**

It should be noted that the number of reports received for different COVID-19 vaccines are not directly comparable as the total number of doses used for each vaccines differ as they were rolled out at different times during the vaccination programme.

The most frequently reported serious AEFIs reported were shortness of breath, chest pain, palpitations and anaphylactic reaction. The majority of these serious cases require only **short-term hospitalisation for treatment or further observation and at the time of AEFI reporting, the affected recipients have recovered or in the state of recovering.**

It should be stressed that the causal link of the event to the vaccination in these reports has not been ascertained meaning that the vaccine does not necessarily cause the serious event, as explained in the Introduction Section.

Out of 1,652 serious AEFI reports, 569 are fatal cases **(0.01 per 1,000 doses)**. Up to 31st.December 2021, after JFK's evaluation based on the investigation findings, none of the fatal outcome reported among the vaccine recipients could be directly linked to the vaccination.

COVID-19 *vaccination in the age of 12 to 17 years*

The vaccines roll-out of PICK-Adolescents for children under 18 years old in Malaysia has started on 20th September 2021. Over 5.6 million doses of Comirnaty and CoronaVac vaccines have been administered in this group. As of 31st December 2021, NPRA has received 1,278 AEFI reports (0.2 reports per 1,000 doses). The most commonly reported reactions include acute stress reaction (239), fever (236), chest pain (175), shortness of breath (165) and palpitations (136).

Higher rate of reports on myocarditis/pericarditis was observed in this group of recipients at 5 cases per 1 million doses administered (in adolescents). Most of the cases were mild in nature and the vaccine recipients responded well to the treatment and recovered/recovering at the time of reporting. This is in accordance with the clinical trials and post-marketing surveillance being conducted elsewhere to date.[5,7-8]

Booster doses

The Comirnaty, CoronaVac and AstraZeneca vaccines have been approved for use as boosters in adults. It is not expected that the type of side effects will be different to first and second vaccine doses based on the results of clinical trials and observations in other countries where booster doses have been rolled out earlier.[5,7-11]

Up to 31st December 2021, we have received 812 reports (0.14 reports per 1,000 doses administered) following the use of boosters, of which 38 of reports **(0.007 reports per 1,000 doses administered)** are categorised as **serious.** This is lower than the AEFI reporting rate for COVID-19 vaccines for all vaccine doses combined. The types of reactions experienced after a booster dose were also found to be similar to those experienced after primary doses, including in heterologous vaccination. The most common side effects reported include fever (200), headache (115), acute stress reaction (106), injection site pain (91) and muscle pain (88), dizziness (69) and shortness of breath (65). Review of booster dose

AEFI reports at this point of time does not raise any new safety concerns. NPRA will continue to closely monitor AEFI data following the use of boosters.

Adverse Events of Special Interest

NPRA is also closely monitoring the occurrences and outcome of specific adverse events known as 'adverse events of special interest', including anaphylaxis, myocarditis/pericarditis, and thrombosis with thrombocytopenia syndrome. These events have mainly been reported in the vaccines clinical trials and post-marketing surveillance globally or observed previously with the use of other vaccines. [5,7-9]

Anaphylaxis is a well-known adverse reaction and the most commonly reported serious AEFI associated with vaccines in general. It usually occurs 15-30 minutes after vaccination. Acknowledging this risk, as part of risk management plan, PICK requires all vaccine recipients to be observed for 15-30 minutes. In rare instances should anaphylaxis reaction occurs, the affected recipient can be treated immediately and effectively.[12]

- During the monitoring period, NPRA had received a total of 100 AEFI reports for anaphylaxis with Covid-19 vaccines equivalent to 1.8 reports per million doses administered. Comirnaty, the mRNA vaccines recorded the highest number of cases at 65 reports or 2.0 per million doses administered. This locally observed rate of anaphylaxis is similar to those reported overseas.[5-,7-9] All anaphylaxis cases were treated accordingly and have recovered/been recovering at the time of reporting.

Myocarditis/Pericarditis is a known but very rare side effect of mRNA vaccines e.g. Comirnaty, especially in male adolescents and young adults.[5,7,13] Symptoms typically include palpitation, chest pain, arrhythmia and dyspnoea. It is usually temporary, with most people getting better within a few days.

- Up to 31st December 2021, NPRA has received 44 reports which have been assessed as likely to be myocarditis/pericarditis following about 32.1 million doses of Comirnaty and two (2) report which have been assessed as likely to be myocarditis/pericarditis from about 4.2 million doses of AstraZeneca administered. This is equivalent to only 14 myocarditis/pericarditis cases reported in every 10 million doses of Comirnaty, although it is more common in male adolescents (8 cases per 10 million doses). Most of the cases were mild in nature and the vaccine recipients responded well to the treatment and recovered/recovering at the time of reporting.

Thrombosis with thrombocytopenia syndrome (TTS) is another known but very rare serious side effect of adenoviral vector COVID-19 vaccines such as AstraZeneca. The exact mechanism of how TTS is triggered is still under investigation, however the majority of cases are associated with the finding of thrombosis location, platelet count, D-dimer and anti-PF4 antibodies.[14] Individuals with TTS generally present symptoms in four (4) to 30 days after vaccination with an adenoviral vector vaccine, which include persistent headaches, blurred vision, difficulty with speech, seizures, and bleeding or bruising.

- Up to 31st December 2021, a total of three (3) cases of TTS were reported following about 4.2 million doses of AstraZeneca. The affected vaccine recipients were hospitalised and have recovered/recovering with treatment at the time of reporting.

Summary

Similar to global scenario[5,7-9], **the vast majority** of the reported AEFIs in Malaysia are **non-serious**.[3] The most common reactions included injection site pain, headache, fatigue, muscle or joint pain, lethargy and fever.

The rate of **serious** AEFIs reported via the NPRA Reporting System is **small at 0.03 per 1,000 doses**, most requiring **short-term hospitalisation for observation and treatment**.[3]

The **benefit-to-risk-ratio** of COVID-19 vaccines registered in Malaysia **remains very favourable**.

NPRA is continuously monitoring the safety of COVID-19 vaccines in the Malaysian population. We encourage all healthcare professionals and vaccine recipients to report any suspected AEFIs. This provides valuable data that helps us to identify new risks and appropriate safety measures and regulatory actions can be taken to mitigate the risk, if deemed necessary. Mostly, however, these events are not caused by the vaccines.

References

1. Ministry of Health, Malaysia. COVIDNOW in Malaysia [Internet]. 2021 [cited 2021 Dec 31]. Available from: https://covidnow.moh.gov.my/
2. Ministry of Health, Malaysia. covid19-public [Internet]. Github. 2021 [cited 2021 Dec 31]. Available from: https://github.com/MoH-Malaysia/covid19-public/tree/main/epidemic
3. National Pharmaceutical Regulatory Agency (NPRA). The Malaysian National ADR database [Internet]. 2021 [cited 2021 Dec 31]. Available from: https://www.npra.gov.my (access restricted).
4. World Health Organization (WHO). Coronavirus disease (COVID-19): Vaccines [Internet]. 2022 Jan 20 [cited 2022 Jan 22]. Available from: https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(covid-19)-vaccines
5. Medicines and Healthcare products Regulatory Agency (MHRA). Coronavirus vaccine - weekly summary of Yellow Card reporting [Internet]. 2022 Jan 20 [cited 2022 Jan 22]. Available from: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting
6. National Pharmaceutical Regulatory Agency (NPRA). The Malaysian Adverse Drug Reaction (ADR)/Adverse Event Following Immunisation (AEFI) Reporting Manual for Healthcare Providers [Internet]. 2021 [cited 2021 Dec 31]. Available from: https://www.npra.gov.my/easyarticles/images/users/1047/Adverse-Drug-Reaction-ADR--Adverse-Event-Following-Immunisation-AEFI-Reporting-Manual-For-Healthcare-Providers.pdf
7. Therapeutic Goods Administration. COVID-19 vaccine weekly safety report - 06-01-2022 [Internet]. 2022 Jan 6 [cited 2022 Jan 22]. Available from: https://www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-06-01-2022
8. Health Sciences Authority. Safety updates on COVID-19 vaccines [Internet]. 2022 Jan 19 [cited 2022 Jan 22]. Available from: https://www.hsa.gov.sg/COVID19-vaccines-safety-updates
9. Uppsala Monitoring Centre (UMC). COVID-19 vaccine reporting in VigiBase. Report 12, data extraction date: 2021-12-16.
10. Hause AM, Baggs J, Gee J, et al. Safety Monitoring of an Additional Dose of COVID-19 Vaccine — United States, August 12–September 19, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1379–1384. DOI: http://dx.doi.org/10.15585/mmwr.mm7039e4external icon
11. Munro APS, Janani L, Cornelius V, Aley PK, Babbage G, Baxter D, et al. Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial. Lancet [Internet]. 2021 Dec 18;398(10318):2258–76. Available from: https://doi.org/10.1016/S0140-6736(21)02717-3

12. Ministry of Health, Malaysia. ANNEX 48: Clinical Guidelines on COVID-19 Vaccination in Malaysia. 3rd ed. [Internet]. 2021 [cited 2021 Dec 31]. Available from: https://covid-19.moh.gov.my/garis-panduan/garis-panduan-kkm/ANNEX_48_CLINICAL_GUIDELINES_FOR_COVID_IN_MALAYSIA_3rd_EDITION_12072021.pdf
13. Marshall M, Ferguson ID, Lewis P, Jaggi P, Gagliardo C, Collins JS, Shaughnessy R, Caron R, Fuss C, Corbin KJE, Emuren L, Faherty E, Hall EK, Di Pentima C, Oster ME, Paintsil E, Siddiqui S, Timchak DM, Guzman-Cottrill JA. Symptomatic Acute Myocarditis in 7 Adolescents After Pfizer-BioNTech COVID-19 Vaccination. Pediatrics. 2021 Sep;148(3):e2021052478. Available from: https://doi.org/10.1542/peds.2021-052478
14. World Health Organization (WHO). Guidance for clinical case management of thrombosis with thrombocytopenia syndrome (TTS) following vaccination to prevent coronavirus disease (COVID-19) [Internet]. 2021 July 19 [cited 2021 Dec 31]. Available from: https://apps.who.int/iris/bitstream/handle/10665/342999/WHO-2019-nCoV-TTS-2021.1-eng.pdf?sequence=1&isAllowed=y

How to report adverse events?

For more information, visit www.npra.gov.my

By reporting suspected adverse events to the NPRA, you help us learn more about the benefits and risks of vaccines – so we can all make better informed decisions.

Always report – so we can learn more about that vaccine and improve how it is used.

For healthcare professionals:

Report adverse events to the NPRA (as healthcare professional) through

- Pharmacy hospital information system (PhIS), OR
- Online web form, OR
- Submission of manual form via mail/email

For consumers:

Inform your healthcare providers at your health facility to make a report on your behalf.

Alternatively, report adverse events to the NPRA (as consumer) through

- Online web form (ConSERF), OR
- Submission of manual form (ConSERF) via mail/email

You are encouraged to first discuss with your healthcare providers regarding the adverse events before reporting directly to NPRA.