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## Monitoring vaccine safety

### Summary points

- Safety monitoring post-marketing allows detection, investigation and evaluation of any new or rare adverse reactions and the safety of a new treatment, including vaccines, in specific population subgroups.
- Safety monitoring post-marketing is part of established regulatory processes. Increased safety monitoring activity is in place in NZ and internationally given the scale of planned COVID-19 vaccination programmes.
- Current data from safety monitoring of the Pfizer vaccine globally is in keeping with clinical trial data showing serious adverse events such as anaphylaxis are rare and effectively managed.
- Increased reporting of coincidental adverse events following immunisation is expected given mass vaccination against COVID-19 of adults who have more co-morbid conditions than children.
- Effective communication with the public about safety monitoring processes and any safety concerns detected is needed and may support overall public confidence about vaccines in use.

### Introduction

The global COVID-19 vaccine rollout which began in December 2020 is continuing at pace in many countries. In the United States, for example, over 189 million doses of COVID-19 vaccines were administered between December 14, 2020, and April 12, 2021 ([link](#)), including over 100 million doses of the Pfizer vaccine.

COVID-19 vaccination commenced in New Zealand on 20 February 2021 and is in the process of scaling up to roll out large-scale community vaccination to the general population from July 2021. Monitoring the safety of vaccines in use from post-marketing data is a usual and a critical process that serves to inform further decision-making as it is needed in relation to vaccine use.

### Systems in Place

Vaccine benefit versus risk evaluation is a continuous process – throughout the life-cycle of vaccine development, and after authorisation of the vaccine for use with post-marketing safety monitoring. Clinical trial data provide extensive information about the safety of vaccines, including any common local or systemic adverse reactions. However, clinical trials are less likely to detect rare adverse reactions and some adverse reactions may only emerge once a vaccine is used by a heterogeneous population over a longer time period ([link](#)). Pharmacovigilance post-marketing is therefore of great importance, and occurs as part of the usual process of medicine and vaccine monitoring post approval. Safety monitoring allows detection, investigation and evaluation of new or rare adverse reactions, the identification of patient risk factors for particular adverse reactions and also, the safety of the vaccine in special population subgroups.

New Zealand has a well-established pharmacovigilance system for collecting and evaluating information on approved medicines and vaccines, and Medsafe oversees this important function. For further information about the vaccine safety monitoring process see the link ([here](#)). Working with Medsafe, the Centre for Adverse Reactions Monitoring (CARM) delivers national pharmacovigilance services for the Ministry of Health, receiving

reports of adverse events following immunisation (AEFIs) from health professionals and the public. Heightened surveillance of the Pfizer vaccine roll out utilising these systems is underway, with an example being the development of a COVID-19 vaccine specific reporting form, available on the CARM website ([here](#)) and more frequent summary reporting of AEFIs ([link](#)). An Independent Safety Monitoring Board has also been established to provide expert advice to CARM, Medsafe and the Ministry of Health on the safety of the vaccine during roll out.

To date, reports of AEFIs following Pfizer vaccination in New Zealand have generally noted minor and transient reactions (such as dizziness, headache, nausea and arm pain) in keeping with clinical trial data. A small number of allergic reactions (including anaphylaxis) have also been reported, with all of these serious reactions effectively managed ([link](#)). Further strengthening of surveillance activity given the scale of the COVID-19 vaccination programme appears warranted. Current ideas being explored include enhancing the communication strategies aimed at encouraging AEFI reporting (e.g. via social media), and the development of a reporting system to follow-up consumers post-vaccination, similar to the AusVaxSafety system used in Australia. Active surveillance systems are formal monitoring systems put in place when relatively new vaccines start being used in a community ([link](#)). The AusVaxSafety is an active safety surveillance system, gathering AEFI data from responses solicited from people post vaccination via automated SMS or email ([link](#)).

## Safety Monitoring: A Global Effort

The Centers for Disease Control and Prevention (CDC) have stated that the overall safety monitoring of the Pfizer and Moderna vaccines since roll out began has been the most intense and comprehensive in U.S. history ([link](#)). A report from CDC of safety monitoring after the first month of administration of the Pfizer and Moderna vaccines covered a period when 13.8 million doses were administered. This concluded that although local and systemic reactions were common, only rare reports of anaphylaxis were received (4.5 reported cases per million doses administered) and there were 'no unusual or unexpected reporting patterns detected' ([link](#)).

In addition to the large number of potential doses involved, the report is notable in that it draws on data from both an existing national passive surveillance system for adverse events after vaccination (the Vaccine Adverse Event Reporting System [VAERS]) and v-safe, an active surveillance system specifically developed for the implementation phase of the COVID-19 vaccination programme. Passive surveillance systems, such as VAERS, are those that involve reporting by health professionals and the public in response to experience of an AEFI. The U.S. V-safe system is another example of an active system and is described as: a smartphone-based tool that uses text messaging and web surveys to provide personalised health check-ins after receipt of a COVID-19 vaccine ([link](#)). It invites members of the public to share their experience of the vaccine with the CDC and gathers large amounts of data.

Reporting from the UK Medicines and Healthcare products Regulatory Agency (MHRA) after 10.9 million doses of the Pfizer vaccine had been administered also showed a similar safety profile to that seen in clinical trials and that severe allergic reactions were very rare (223 cases) ([link](#)). This remains the MHRA assessment in terms of the safety profile of the Pfizer vaccine. For further regularly updated details of MHRA safety reporting on the Pfizer vaccine and other COVID-19 vaccines being used in the UK see this [link](#).

In New Zealand, we have had the advantage of being able to review emerging safety monitoring data from these jurisdictions and elsewhere. We will continue to benefit in terms of safety data, from the scale of the vaccination programmes overseas, compared to that of our own small population. In addition, Phase IV studies and other research, as well as mandatory reporting requirements of the manufacturer, will continue to provide Medsafe

with relevant safety data. Medsafe, in turn, will continue to share our New Zealand experience of the Pfizer vaccine internationally, including through WHO reporting.

## Adverse Events and Public Perceptions

The perceived safety of a medicine or vaccine is a key factor in an individual's decision to use the medicine or vaccine. It is well recognised that AEFIs have the potential to undermine confidence in a vaccine and can potentially have major consequences for overall immunisation coverage and disease incidence, if not dealt with rapidly and effectively ([link](#)). A recent opinion piece in the BMJ expressed dissatisfaction with media reporting of concerns about the AstraZeneca vaccine, citing historical precedents where publicised safety concerns have had a long-lasting impact on vaccine confidence ([link](#)).

Adverse events following immunisation reported do not necessarily indicate causality, as may be construed in some media reporting. The WHO have advised that a higher incidence of coincidental AEFIs should be anticipated with COVID-19 vaccines given that mass vaccination programmes are occurring in adults who have more co-morbid conditions than children (see COVID-19 Vaccines: Safety Surveillance Manual December 2020; [link](#)). However, AEFIs may indicate a potential safety signal – a new finding within safety data that requires further investigation. This is the case for serious adverse events, which are defined by international agreement (ICH ED2 Post-approval safety data management [link](#)) and include any events that are:

- judged as a medically important event or reaction;
- result in significant incapacity or disability;
- require hospitalisation or longer stays in hospital; or
- are life-threatening; or result in death.

Non-serious adverse events may also act as safety signals.

The BMJ opinion piece highlighted the critical importance of health and regulatory bodies such as MHRA, EMA, FDA and WHO [and in New Zealand, Medsafe] in ensuring an evidence-based approach to address such safety concerns. Some of the media reporting on the AstraZeneca vaccine may have been misleading and harmful. However, in the context of mass vaccination, heightened media interest is inevitable and in the context of serious adverse events, a robust discussion is a 'public good'. Transparency in sharing relevant information about safety monitoring processes, as well as findings, may potentially assist in maintaining overall public confidence in the safety of the vaccines.

## Concluding Comments

Any new information that changes the balance between benefit and risk of harm may affect the acceptability of a vaccine, or medicine. In addition, the evaluation of this balance may change over time as new information becomes available.

As the New Zealand vaccination programme using Pfizer continues to roll out, data from millions of doses of the vaccine given overseas gives ground for confidence. Safety monitoring of the vaccine also continues both here and internationally as part of established regulatory processes providing ongoing safety data for analysis. Communication with the public about vaccine safety monitoring activity, in general, can influence vaccine acceptance. More communication around progress on this topic may be beneficial, along with effective

communication about any specific safety signals should they arise. Together, this may serve to help maintain public confidence in the vaccination programme as a whole.