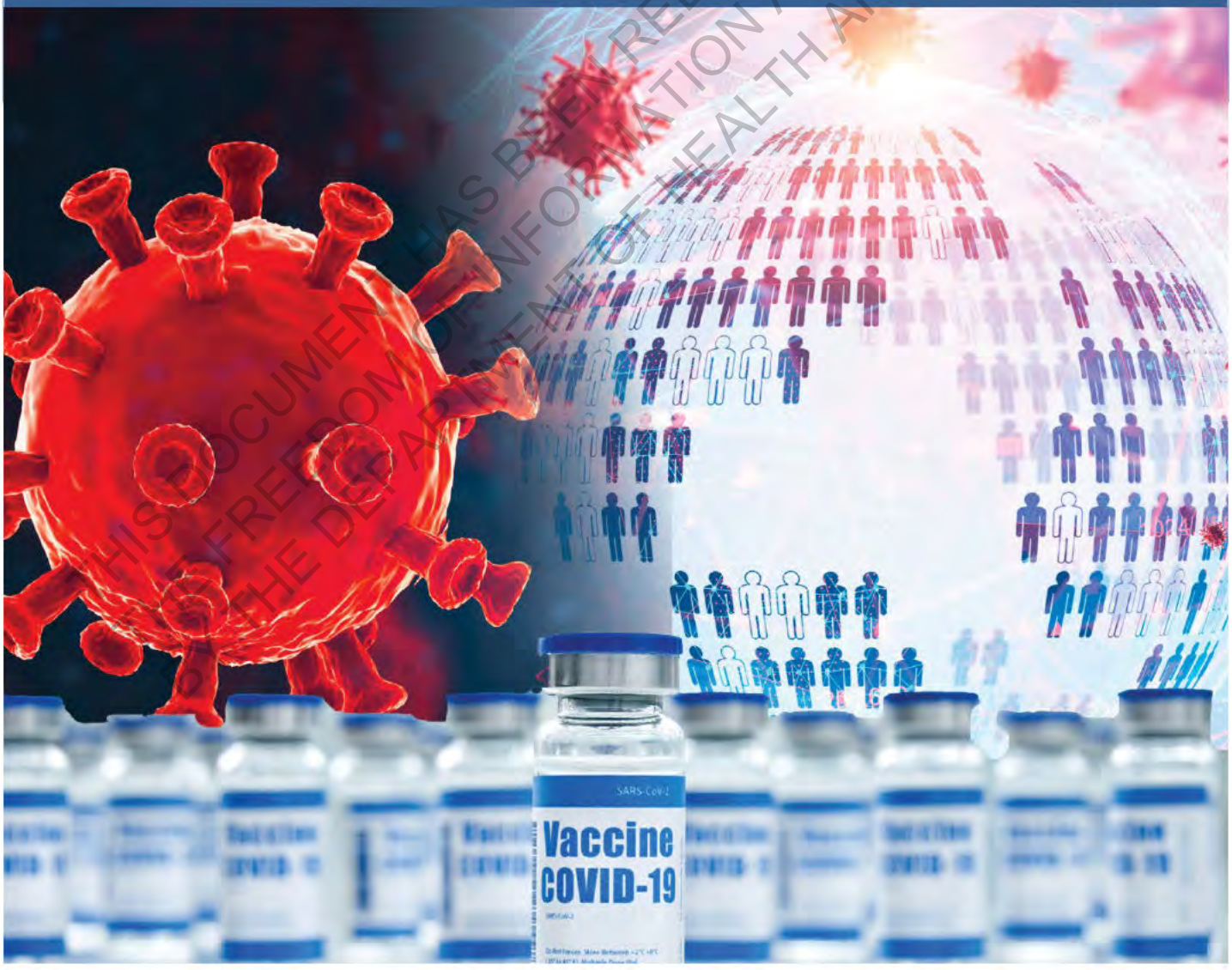
Review of COVID-19 Vaccine and Treatment Purchasing and Procurement



The Hon Mark Butler
Minister for Health and Aged Care
Parliament House
CANBERRA ACT 2600

Dear Minister

On 30 June 2022 you commissioned an independent review of the purchasing and procurement of COVID-19 vaccine and treatments to inform the next 12-24 months. This report provides the conclusions and recommendations of the review.

The review team engaged with a number of key stakeholders involved in Australia's response to the COVID-19 pandemic and rollout of vaccines and treatments. This included epidemiological experts both nationally and internationally, Commonwealth, state and territory Health departments and bodies, health sector organisations, as well as manufacturers of the vaccines and treatments procured within Australia.

As principal reviewer I was assisted by Professor Peter Collignon AM who provided expert medical advice. I would also like to acknowledge the work of the review project team led by Georgie Fairhall, Department of Health and Aged Care.

Early procurement of vaccines and treatments occurred in a highly competitive global market. In this context Australia secured a portfolio of effective COVID-19 vaccines and treatments enabling high rates of primary course vaccination preventing serious illness and death relative to global peers.

However, Australia and the world are not yet 'COVID-stable', and we are unable to confidently predict the timing or impact of new waves and variants. This uncertainty presents particular challenges. The availability of efficacious vaccines and treatments will continue to play a key role in ensuring ongoing protection for lives and livelihoods

The next two years are critical to supporting our economy, health and education systems to recover. Australia's approach to the procurement of vaccines and treatments needs to be responsive to the changing environment and should be guided by clear policy and understanding of risk appetite.

Consideration should be given to the decision-making structures and advice required, and whether new and existing pathways for procurement and distribution of vaccines and treatments should be retained or adapted. Finally, it is critical that Australia maintains surge capacity in the event of a serious new variant or another infectious disease.

Yours sincerely

Hon. Professor Jane Halton AO PSM
19 September 2022

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Attachments

~ This report contains commercial in confidence material which should not be released without authorisation ~

1. Executive Summary

On 30 June 2022, the Minister for Health commissioned a rapid review of the procurement and distribution of COVID-19 vaccines and relevant therapeutic goods to ensure that Australia has sufficient supplies to meet immediate and prospective needs including for the next 12 – 18 months. See Terms of reference at Attachment 1.

Like many other countries, Australia is at an important point in the evolution of the SARS-CoV-2 pandemic. Management of the health and economic effects of continuing waves of infection has shifted to more permissive settings largely enabled by widespread vaccination and natural immunity from infection. Previous emergency settings have been replaced by individual responsibility for isolation in the event of infection. These more liberal settings have been widely welcomed by the community.

Unlike the early phases of the pandemic a range of treatments is also now available.

This new phase of the pandemic brings new challenges. We are not yet 'COVID-stable' and cannot reliably predict when new waves or variants might emerge. The ability to rapidly deliver effective vaccines and therapies to large numbers of people will remain relevant to planning and procurement for some time to come. There will continue to be a need for supply agreements and delivery arrangements that are effective and have the capacity to scale for spikes in demand.

In the medium term, hopefully, there is more stability/predictability in respect of SARS-CoV-2 allowing this virus to be managed much like other respiratory viruses (such as influenza). This will require a review of those systems to ensure that they are fit for purpose including ensuring ordering and delivery arrangements are responsive to demand and the specific needs of COVID-19 vaccines and treatments.

In the event a new and significantly different variant with severe health outcomes emerges, the capacity to respond rapidly and at scale should remain a policy and delivery priority.

This report outlines findings and recommendations in respect of current and future vaccine and therapeutic availability, the development pipeline, and priorities for procurement. This will ensure that Australians can access effective vaccines and therapies if/when needed to protect against infection and help prevent severe disease and death at a time of continued widespread COVID infection with new SARS-CoV-2 variants.

These observations and conclusions should inform current negotiations for immediate and future purchases of both vaccines and therapies. Current and potential distribution mechanisms together with advisory mechanisms are also considered.

Prior purchases are considered only to the extent these are relevant to existing and future supply and the lessons that can be learned in respect of fit for purpose supply and procurement arrangements going forward.

1.1 Conclusions

COVID-19 Pandemic

- It is not possible to accurately predict the further evolution of the virus and Australia is likely to continue to be challenged, at least in the short term, by emerging variants and new waves of disease.

Australia in context

- Australia has been successful at achieving high rates of primary course vaccination and maintaining a low death rate, but relative performance is beginning to wane.

Regulation of vaccines and treatments

- Where appropriate, Australia should continue to look for opportunities to ensure consistency with global regulators. Consideration should be given to permanent implementation of changes made during the pandemic which ease regulatory burden and do not impact public safety.
- Funding available to the TGA should enable it to continue its important work regarding pharmacovigilance and consumer safety.

Policies, decision-making and advisory mechanisms

- The need to mitigate the effects of COVID-19 is likely to remain. However, policy settings have not been updated to take account of already widespread COVID-19 infections and associated high levels of hybrid immunity, the possibility of future waves and variants, and developments in vaccine and therapeutic science and manufacturing. A portfolio approach and potentially redundancy will be needed to ensure access.
- This context continues to present real challenges in decision-making in respect of procurement of, eligibility for, and distribution of both vaccines and treatments. Supply chain issues remain with potential shocks or spikes in demand hard to estimate.
- Pre-pandemic structures and processes were not fit for purpose in an emergency context. With the likelihood of continuing waves of COVID-19 and the need for ongoing, integrated advice, new advisory structures and mandates will be required. It is timely to consider the role and nature of existing structures and processes. The *ad hoc* arrangements put in place at the beginning of pandemic require updating.

COVID-19 Vaccines

- Australia's procurement activities were consistent with other high-income countries. A portfolio and redundancy approach was adopted to mitigate risks and ensure adequate supply.
- Early procurement of vaccines and treatments occurred in the context of uncertainty and a global vaccine shortage – a “sellers' market”. Agreement to conditions not usually included in ordinary procurement contracts was necessary to secure commitments to supply.
- A portfolio approach will continue to be needed to mitigate the risk of supply shortage, delays, lack of success in clinical trials, manufacturing or regulatory failure.
- Delivery requirements for consumables are much less onerous than for vaccines. Current delivery arrangements should be reviewed to ensure value for money.
- In order to maximise coverage and reduce confusion it is important to:
    - clarify who the key decision-maker on vaccine eligibility is and which bodies act in an advisory capacity;

- avoid complexity in eligibility criteria where there is no significant clinical difference between cohorts to ensure high levels of public awareness and vaccine uptake; and
- align key public messaging, public health goals, and high-level COVID-19 vaccine policy.

- The proportion of vaccines administered by state and territory hubs has decreased over time with general practice and pharmacy now administering most vaccines. The ability to quickly stand-up mass vaccination clinics should be retained in the event of an emergency or period of high demand.
- Wastage is expected in an oversupply environment. Eligibility and priority use recommendations can affect wastage.
- New variant specific, bivalent, and more broadly protective vaccines are being researched and developed.
- Initial trial data, based mainly on antibody responses, show that variant specific vaccines may be more effective than the original wildtype vaccines against Omicron variants.

COVID-19 Treatments

- Australia has procured a range of treatments which are available through state hospitals and community pharmacy. It is important to continue to monitor the ongoing efficacy of COVID-19 treatments against the current dominant strains and latest clinical research.
- A systems approach to distribution and clear communication to patients about eligibility and access is needed to ensure available treatments are utilised to mitigate the impact of COVID-19.
- With considerable disruption to work and education still being experienced, the potential benefit of wider use of efficacious treatments (particularly where there are sunk costs) should be considered.
- Some wastage of therapeutics is to be expected as stock begins to expire due to slower than anticipated utilisation and treatments losing efficacy against current variants.
- Ongoing monitoring of COVID-19 mutations and variants, including impacts on treatment efficacy, will be required.
- Significant stocks of treatments are available. These should provide adequate cover for the next 12 months however mechanisms to scale up supply in the event of high or emergency demand are needed.

Transitional arrangements

- Policies, procurement, and delivery over the next two years should:
  - Encourage ongoing high levels of vaccination across the community for those that will benefit;
  - Enable the Health Minister to operate in the transition period (before 'COVID-stable' is achieved) to manage the downside risk associated with the emergence of a serious new variant;
  - Ensure that there is adequate and speedy access to vaccines and treatments by patients, if and when they are required;
  - Provide maximum possible protection through vaccinations and treatments over the short to medium term to protect the vulnerable, limit hospitalisation and death, and allow the economy and health system to recover;
  - Adopt a portfolio and redundancy approach to the procurement of vaccines and treatments, with acceptance of associated higher levels of wastage;

- Encourage a partnership approach with industry and sponsors ensuring transparency and optimal outcomes for Australian patients;
- Utilise existing and established distribution channels (primary care including general practice and pharmacies, and states and territories) and maintain capacity to ensure distribution of vaccines can be scaled up rapidly in the event of a need for high levels of vaccination for a new more virulent variant; and
- Facilitate decision-making which considers the ongoing public health management of the pandemic rather than the point in time relative risk (e.g. absolute risk of side effects as determined by TGA/medical analysis). Unless there are significant clinical differences, approaches should be simplified as much as possible to streamline and encourage public uptake.

Vaccines

- Forecasting required numbers of vaccines is an inexact science. Clear policy positions, risk frameworks, and understanding of the development pipeline, production issues, demand and delivery arrangements is needed to inform judgement and guide decision-making.
- On-demand ordering arrangement would significantly reduce the wastage of vaccine products in low and medium demand scenarios, and therefore reduce the total amount of vaccines required to meet demand in 2023 and 2024.
- Australia will likely have an over-supply of Novavax in 2023. Australia could implement more permissive eligibility settings for Novavax to increase uptake and reduce the need for additional mRNA vaccines; and/or work with the manufacturer to defer delivery of doses into 2024.
- Additional procurement of Moderna vaccines should be undertaken for 2023 to meet any anticipated shortfall in the number of mRNA vaccines required and to ensure access to vaccines for children under five years.
- Minimum endemic, 'COVID-stable', quantities of effective vaccines should form the foundation of 2024 vaccines orders. In the event 'COVID-stable' has not been achieved a prudent buffer should be based on medium demand options. Specific arrangements to scale up supply in the event of high or emergency demand should be designed and implemented.
- Global supply of any new effective variant specific and/or broadly protective vaccines will be constrained for some time once approved by regulators. Early purchases will continue to be made in a highly competitive market. Flexible APAs are required to navigate the procurement environment and ensure adequate supplies of vaccines in Australia. Existing APAs and supply agreements provide a starting point for negotiations.

Treatments

- Ongoing monitoring of new treatments and engagement with suppliers will be needed to ensure adequate supply of promising emerging treatments for Australia.

1.2 Recommendations

Recommendation 1: Public health campaigns designed to encourage sustained booster uptake for those that will benefit should be developed and delivered during 2023 and 2024 to improve coverage.

Recommendation 2: A clear, updated, policy framework including objectives for the management of COVID-19 should be developed to inform decision-making, purchasing, clinical decision-making and resource allocation. A statement of risk appetite should form a part of this framework.

Recommendation 3: Advisory structures should be streamlined, and advice should be integrated to enable decision-makers to undertake their role. The role of decision-makers and advisors should be clarified. Reasons for decisions should be evidenced including indicating where they are based on judgment. Care should be taken to prevent confusion at the clinical level about who is eligible to receive vaccines/treatments and recommendations for use including in respect of target populations.

Recommendation 4: Procurement decisions should be made in the context of agreed policy objectives, risk appetite (the acceptability of failure to supply), knowledge/predictions in respect of the evolution of the virus, and supply constraints including knowledge of market behaviour.

Recommendation 5: Vaccine distribution arrangements should be reviewed in order to test value for money and reduce wastage while ensuring timely access.

Recommendation 6: New mechanisms to manage stock held by the NMS for use in an ongoing pandemic or epidemic should be developed as a matter of urgency to enable greater transparency about and access to stock held.

Recommendation 7: The Department of Health and Aged Care should work with sponsors to ensure that adequate supplies of therapeutics are available to meet reasonably anticipated demand for the next two years. Mechanisms such as guarantees for minimum supply should be explored to ensure availability and access.

Recommendation 8: Steps should be taken, consistent with an agreed policy and risk appetite, to ensure adequate supplies of vaccines and treatments are available across 2023 and 2024 including in the event of spikes in demand. This should include additional Moderna vaccines in 2023 and, as a minimum and based on an assessment of 'COVID-19 stability', doses necessary to meet baseline demand in 2024.

2 COVID-19 Pandemic

The emergence of a novel coronavirus was reported in late 2019 in Wuhan, China. Severe acute respiratory syndrome coronavirus two (SARS-CoV-2) spread rapidly resulting in a 'public health emergency of international concern' due to high rates of transmission and associated high mortality. A global pandemic was declared on 11 March 2020.[1]

The virus, which causes the disease known as COVID-19, has a genetic sequence like the corona viruses which cause of common cold syndromes, as well as viruses which cause more severe disease, such as the Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) viruses.[2] COVID-19 causes flu-like symptoms with a wide range of severity across infected patients.[3]

[1] T Ghebreyesus, 'WHO Director-General's opening remarks at the media briefing on COVID-19', *World Health Organization*, 11 March 2020, accessed 10 August 2022.
[2] F Amanat and F Krammer, 'SARS-CoV-2 Vaccines: Status Report', *Immunit*, 2020, Vol. 52. 4 s.l.
[3] W Guan et al., 'Clinical Characteristics of Coronavirus Disease 2019 in China', *NEJM,* 2020, Vol. 382, pp. 1708-1720.

While most COVID-19 cases present with mild to moderate symptoms prior to vaccination, approximately 20% of cases are severe with severe symptoms mostly occurring in individuals aged 50 years or older.[2] In most unvaccinated age groups, the severity of the disease is much greater than that of the seasonal influenza. Case fatality is also age dependent resulting in a higher fatality rate in older people.[2]

In those unvaccinated and over the age of 80 years, the case fatality rate is over 10%. COVID-19 illness is generally milder in children and is often asymptomatic. The frequency of severe illness from COVID-19 is lower in adolescents than in adults, with approximately 4% to 7% of adolescents experiencing severe outcomes.[4] Across all ages, the Infection Fatality Rate (IFR), or the likelihood of mortality from infection prior to vaccination, is estimated between 0.5% and 1%.[5] Most deaths contributing to the IFR occur in those over the age of 70 years.

Globally, approximately 603.56 million cases of COVID-19 have been confirmed and at least 6.49 million people have lost their lives to the disease as of 2 September 2022[6]. Australia has recorded 10.06 million COVID-19 infections and 14,053 deaths. While the Australian death rate is low compared to many other countries, the loss experienced by friends and families has been significant.

Since the emergence of COVID-19 in late 2019, the SARS-COV-2 virus (the virus) has mutated many times. The original strain (ancestral) has been overtaken by new variants with increased viral fitness and immune evasion.[7] Some of these new variants have significantly greater infection rates. Resulting spikes in cases have led to multiple waves of the pandemic.

By January 2021, the Omicron variant had emerged as the dominant variant, accounting for most new infections. The dominance of Omicron is evident through the large number of sub-variants. Currently, the subvariants BA.4 and BA.5 are the most common. Researchers suggest that new subvariants, potentially evolving from the BA.2 or BA.5 families, will continue to emerge and drive new infections.[8]

Initial research indicates that immunocompromised individuals who have long-lasting COVID-19 infections may drive the emergence of new variants at higher rates, highlighting the importance of protecting vulnerable members of the community from infection.[9]

Scientists are not able to predict when new variants will emerge in the community, or what traits these variants will have. It is also unclear what level of infectiousness or severity new variants may have. In addition, new variants may continue to develop "immune escape" abilities that are present in the Omicron variant, which increases infectiousness and reduces the efficacy of existing vaccine products.

s47C, s34(3)

[4] E Molteni et al., 'Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2', 2021, *The Lancet Child & Adolescent Health*, Vol. 5, pp. 708-718.
[5] B Salzberger et al., 'Epidemiology of SARS-CoV-2', *Infection*, 2021, Vol. 49.
[6] Our World in Data, 'Coronavirus (COVID-19) Cases', *Our World in Data,* accessed 6 September 2022.
[7] K Tao et al., 'The biological and clinical significance of emerging SARS-CoV-2 variants', *Nature Reviews Genetics,* 2021, Vol. 22, pp. 757–773.
[8] S Duchene and A Porter, 'Why are there so many new Omicron sub-variants, like BA.4 and BA.5? Will I be reinfected? Is the virus mutating faster?' [Online] *Doherty Institute*, 06 May 2022, accessed 09 August 2022.
[9] K Kupferschmidt, 'As Omicron rages on, scientists have no idea what comes next', *Science*, 2022, Vol. 377. 6604.

It is not possible to accurately predict the further evolution of the virus and Australia is likely to continue to be challenged, at least in the short term, by emerging variants and new waves of disease.

2.1 Management of COVID-19

Early management of COVID-19 saw countries adopt a public health approach. Waves of infection placed significant pressure on acute care settings, such as those seen in outbreaks in Italy and the United States (US), and widespread restrictions were implemented.

Significant restrictive public health orders were enacted across OECD (Organisation for Economic Co-operation and Development) countries and economies shrank by between 1.7% and 10.4% in the March and June quarters in 2020.[10]

As was the case during the 'Spanish Flu' pandemic, the absence of effective vaccines and treatments meant that implementation of public health measures and the provision of infection control advice to citizens were the only options available to policy makers and public health officials.

Some countries chose to implement 'COVID-zero' or suppression strategies that involved closed domestic and international borders, physical distancing rules and lockdowns, and mandating the use of facial coverings to reduce the spread of the disease. As new variants emerged new measures were adopted. These were necessitated by the evolution of the virus.

Australia's first case of COVID-19 was confirmed on 25 January 2020, travel restrictions were introduced on 1 February 2020, the Government declared a biosecurity emergency on 18 March 2020, and Australia's borders were closed on 19 March 2020.

Australia introduced measures such as stay at home orders (including for school students), forced closure of businesses, and restrictions on gatherings. These policies aimed to reduce the reproduction rate of the virus allowing health systems to implement strategies to manage the surge in infection and associated serious illness to minimise deaths.

Strict enforcement of and community compliance with public health measures including quarantine, border closures, lockdowns, and mask wearing allowed Australia to perform well early in the pandemic. Relative to comparable countries, a low cumulative death rate of 34.99 deaths per million people was achieved by 31 October 2020 compared to other countries including Israel (275.64), US (683.95), and the United Kingdom (UK) (954.47).[11]

Countries have now largely moved away from 'COVID-zero' or suppression strategies due to the protection vaccines have provided from death and serious illness, and the availability of treatments, which have been targeted at those with risk factors and vulnerable groups. Current international approaches to COVID-19 management are detailed in Attachment 3.

The eventual widespread availability of effective vaccines and vaccine mandates meant that Australia achieved high rates of vaccination (once vaccines became available and eligibility was expanded).

[10] OECD (2022), 'Quarterly GDP (indicator)', *OECD,* doi: 10.1787/b86d1fc8-en, accessed 16 August 2022.
[11] Our World in Data, 'Coronavirus (COVID-19) Deaths', *Our World in Data,* accessed 6 September 2022.

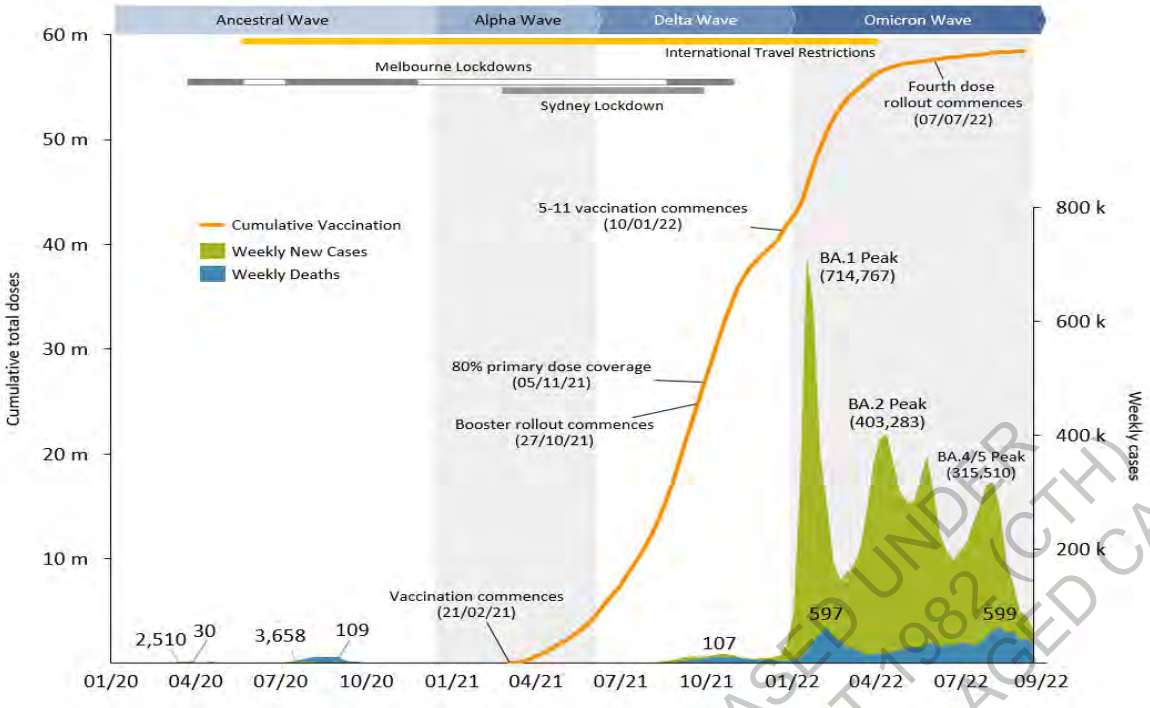


Figure 1: Australia's COVID-19 response and outcomes.[12]

The weekly death rate in Australia peaked in waves in line with the arrival and spread of COVID-19 variants of concern. The highest weekly death rate per million in Australia occurred in late January of 2022 during the Omicron wave, with peak of 3.37 (compared to the peak of 0.59 during the Delta wave).[13] At 2 September 2022, Australia's cumulative death rate per million reached 542.14, which remains lower than that of comparable countries (see Figure 2). However, the current weekly death rate per million in Australia is 12.31, greater than the weekly rates in the US (10.41), the UK (10.21) and New Zealand (8.97).[14]

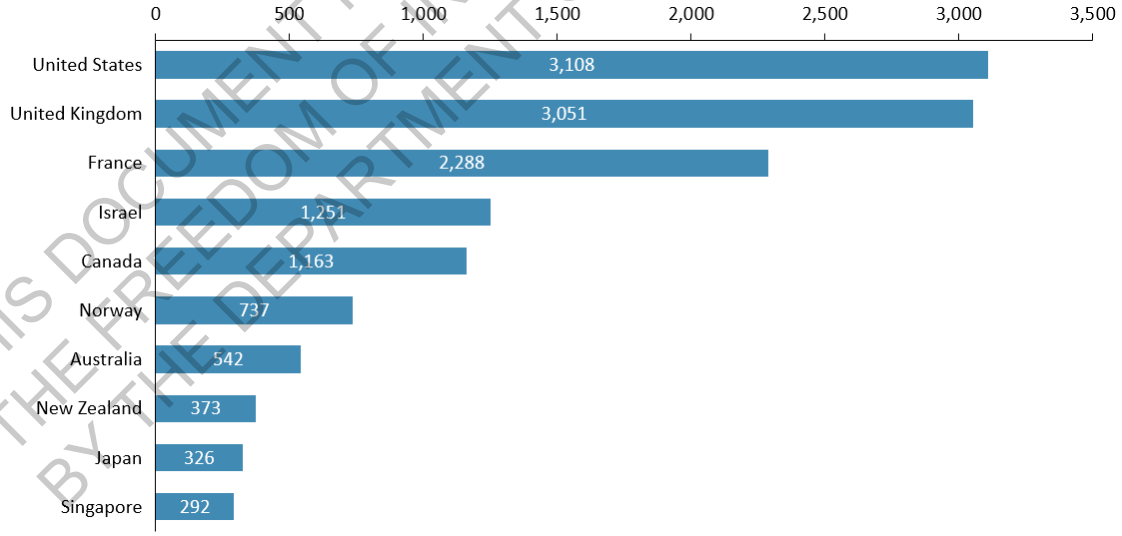


Figure 2: Cumulative confirmed COVID-19 deaths per million people by country.[15]

[12] Our World in Data, 'Coronavirus Pandemic (COVID-19)', *Our World in Data,* 2 September 2022, accessed 7 September 2022.
[13] Our World in Data, 'Coronavirus (COVID-19) Deaths', *Our World in Data,* 2 September 2022, accessed 6 September 2022.
[14] Our World in Data, 'Coronavirus (COVID-19) Deaths', *Our World in Data,* 2 September 2022, accessed 6 September 2022.
[15] Our World in Data, 'Coronavirus (COVID-19) Deaths', *Our World in Data,* 2 September 2022, accessed 2 September 2022.

While global economies have rebounded and people have established 'COVID-normal' ways of living, virus variants have rendered existing vaccines less effective at preventing transmission of the disease. Consequently, high infection rates continue to cause lingering disruption to health systems, education systems, and supply chains.

There are still significant unknowns regarding the evolution of SARS-CoV-2 and countries will need to continue to actively manage the impact of the virus. Optimising uptake of vaccines and treatments and investing in new vaccines and treatments (where more effective) in what will remain a highly competitive global market will be critical.

2.2 Vaccines and Treatments

The genetic sequence for SARS-CoV-2 was made available to the world in early January 2020. This was a necessary precursor to the development of vaccines.

Despite previous knowledge of serious infection syndromes caused by Coronaviruses such as SARS and MERS, no effective human Coronavirus vaccine had ever been developed. Existing work on these pathogens was, however, material to success in respect of SARS-COV-2.

Similarly, there were no treatments available in early 2020 targeting the novel virus.

Global experts commenced development of vaccines and treatments immediately but cautioned that production of effective products requires care and time. Success was not guaranteed. The global scientific and funding community, including not for profits, private sector, and government investors took multiple 'shots on goal' and poured significant resources into developing vaccines in record time. This included the use of multiple platforms (for vaccines) and the investigation of both existing and new therapies as potential prophylaxis and treatment options.

Development of a successful vaccine is typically a long and expensive process (see Figure 3). Each vaccine candidate must pass multiple stages of clinical trials, data analysis, and processing checks to ensure efficacy and safety before they can seek regulatory approvals prior to being offered to the public.[16]

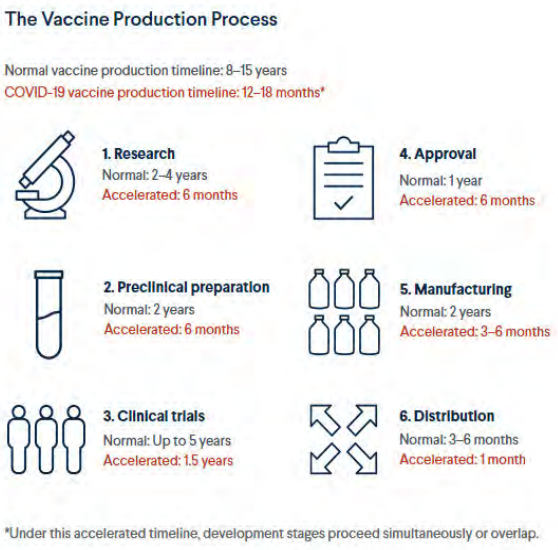


Figure 3: The vaccine production process.[17]

[16] A Uttarilli et al., 'Super-rapid race for saving lives by developing COVID-19 vaccines', *Journal of Integrative Bioinformatics*, 2021, Vol. 18, pp. 27-43.

[17] C Klobucista, 'A Guide to Global COVID-19 Vaccine Efforts', *Council on Foreign Relations*, 19 July 2022, accessed 11 August 2022.

By mid-2020, five vaccines had entered Phase I clinical trials by April 2020 and early clinical successes were reported. While normal vaccine development may take 10 years or more before public use commences, new approaches to development were utilised to accelerate development and decrease production time including new technologies, bioinformatics and parallel studies with extensive global cooperation.

During the pandemic a 'speed premium' was paid by vaccine developers. While some investments would not prove effective (funding was made available at significant risk), the time to produce vaccines was significantly reduced. As a result, vaccine products were able to enter phase I trials less than 10 weeks after the first genetic sequences of SARS-CoV-2 was released.[18]

By May 2020, just four months after the virus was identified, more than 120 vaccines were in the global development pipeline. Due to the risks associated with vaccine development, not all these candidates would prove fruitful. Simultaneous research into alternate product types and development processes has been considered key to ensuring access to successful candidates.[19]

Vaccine uptake was slow in the beginning phases of global vaccination programs due in part to shortages in both supply, labour, and materials. In the early stages of the rollout, high income countries were significantly advantaged due to prospective supply agreements struck in 2020.

Countries with significant vaccine/treatment research, development, and production ecosystems were also relatively advantaged. This included focussed effort on counter measures, including through existing specialised agencies such as the Biomedical Advanced Research and Development Authority (BARDA) in the US, directed towards countering SARS-COV-2 and leveraging manufacturing systems.

Global vaccination coverage and production grew significantly over 2021, with 11.6 billion doses manufactured. Global vaccine coverage is 62.21% (two doses) as at 2 September 2022. However, this obscures the difference between coverage in high income countries (73.74%) and low-income countries (17.05%).[20] Gavi is forecasting between 9.7 billion and 13.9 billion doses will be manufactured in 2022.

Globally, the most procured vaccines are Pfizer (~6.5 billion doses), AstraZeneca (~3.5 billion doses), Moderna (~2 billion doses), and Novavax (~1.3 billion doses).[21]

As with vaccines, there were no treatments for COVID-19 during the early stages of the pandemic.[22] Researchers globally undertook numerous *in vivo*, *in vitro* and *in silico* studies to identify promising treatment options to halt disease progression in infected individuals. These treatments were also expected to play a vital role in lowering infection rates and hospital admissions, reducing burden on health systems, and decreasing transmission in vulnerable patient groups.[23]

Common strategies leading to rapid discovery of COVID-19 treatments included screening of large existing compound libraries, testing and repurposing of existing broad spectrum antiviral agents, and *de novo* development of novel treatments such as monoclonal antibodies based on current knowledge and understanding (e.g., pathogenesis and replication mechanism) of SARS-CoV-2.[24]

[18] A Uttarilli et al., 'Super-rapid race for saving lives by developing COVID-19 vaccines', *Journal of Integrative Bioinformatics*, 2021, Vol. 18, pp. 27-43.
[19] A Uttarilli et al., 'Super-rapid race for saving lives by developing COVID-19 vaccines', *Journal of Integrative Bioinformatics*, 2021, Vol. 18, pp. 27-43.
[20] Our World in Data, 'Coronavirus (COVID-19) Deaths', *Our World in Data,* accessed 5 September 2022.
[21] UNICEF, 'COVID-19 Market Dashboard', *UNICEF,* 6 September 2022, accessed 6 September 2022.
[22] M Cascella et al., 'Features, Evaluation, and Treatment of Coronavirus (COVID-19)', *StatPearls,* 2022
[23] K Bliss, S Morrison, 'COVID-19 Therapies at the Crossroads', *Center for Strategic & International Studies,* 2022, 06 July 2022, accessed 16 August 2022.
[24] A Zumla et al., 'Coronaviruses - drug discovery and therapeutic options.', *Nat Rev Drug Discov*, 2016, 15(5): p. 327-47.

Currently, most COVID-19 treatments approved for use locally and internationally are either anti-SARS-CoV-2 monoclonal antibodies or antiviral agents.

The SARS-CoV-2 virus and mutations are difficult to combat as they are highly infectious and also have genetic variability that leads to high antigenic variation resulting in the emergence of drug resistant strains of the virus, such as that seen against monoclonal antibody treatments.[25] Therefore, it is important to have multiple treatment options to manage ongoing and potential future pandemics for SARS-CoV-2.

Pivotal clinical studies undertaken by sponsors of current COVID-19 treatments were conducted pre-Omicron in mostly unvaccinated populations. s47C, s34(3)

Changes in the dominant SARS-CoV-2 variant also influences the efficacy of medicines and vaccines. These changes are significant for decision-making and the relative benefit of individual vaccines and treatments will continue to need to be assessed. For example, if the immune response generated by vaccination or infection provides suboptimal protection against a new variant, the potential efficacy of COVID-19 treatments may have a proportionally greater public health benefit due to increased infections and less immune protection.

Similarly, the availability of new vaccines which more effectively protect against (re)infection, severe disease, and death will be important in managing COVID-19 going forward if/when they become available and would therefore have a high cost-benefit.

3 Australia in context

Australia's early decisions to close boarders and implement significant public health mandates undoubtedly saved many lives. Months spent 'COVID-free' in most jurisdictions meant that much of the population lived largely unaffected. However, these periods were interspersed with sporadic geographic lockdowns, tough quarantine requirements, and internal boarder closures, most notably the extended lockdowns in Melbourne. Movements were severely restricted within and across Australia.

The total effect of the Australian response (including achieving high levels of vaccination before wide spread of the virus) can be seen in the very low number of cumulative COVID-19 deaths per million people relative to the rest of the world (see Figure 2). The cost of these measures both in dollar terms and other measures, such as broader economic, educational, and mental health impacts, is yet to be calculated or fully realised. The Commonwealth, states and territories all provided significant support to the population throughout the pandemic. See Attachment 3.

One effect of this long period of comparative success in limiting the number of cases for the early part of the pandemic is the currently relatively higher death rate due to the current Omicron wave. Notwithstanding very high rates of primary vaccination, waning immunity and a population largely unexposed to widespread infection has seen a spike in deaths over Australia's winter. This death rate is now falling as the spread of Omicron is decreasing and our winter ends (see Figure 4).

[25] D Focosi et al., 'Monoclonal antibody therapies against SARS-CoV-2.', *The Lancet Infectious Diseases*, 2022.

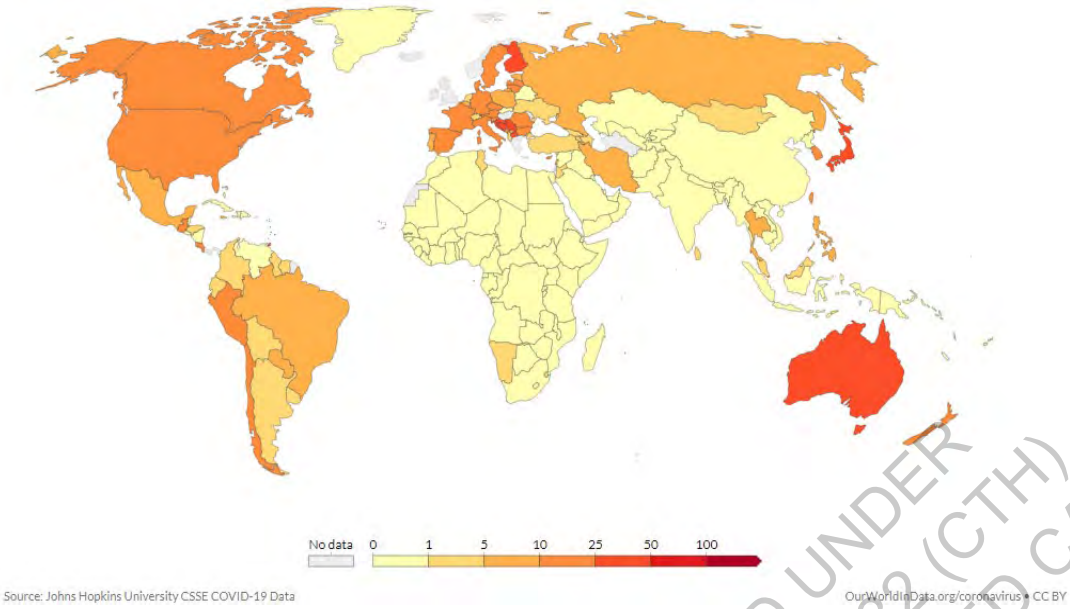


Figure 4: Average confirmed COVID-19 deaths per million people over a two-week period by country.[26]

In Australia, there are three types of vaccine available which each have different mechanisms of action to induce an immune response: viral vector, mRNA, and protein subunit. Each vaccine exposes the patient's immune system to the spike protein marker from the virus which allows it to produce specialised immune cells that will target SARS-CoV-2.[27] An overview of the Australian vaccine types, efficacy, and safety is included at Attachment 4.

Initially, Australia's vaccine rollout and coverage lagged other high-income countries. On 30 June 2021, only 6% of eligible Australians had been fully vaccinated compared to 56% of people in Israel and 49% of the respective populations in the UK and US (see Figure 5).

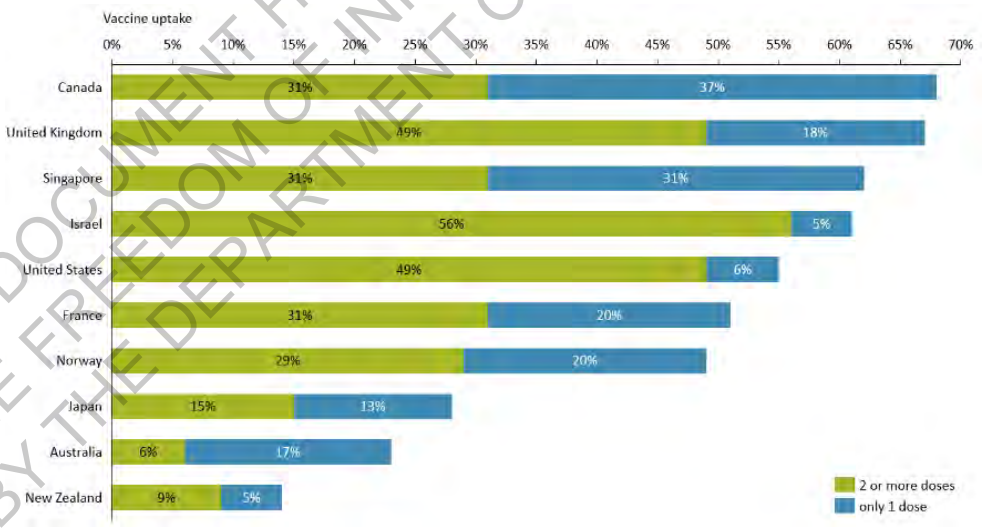


Figure 5: People vaccinated by country at 30 June 2021.[28]

[26] Our World in Data, 'Biweekly confirmed COVID-19 deaths per million people', *Our World in Data,* 2 September 2022, accessed 6 September 2022.
[27] P Doherty, 'Issue #84 Viruses, Vaccines and COVID-19: arming up', *Doherty Institute*, 22 November 2021, accessed 11 August 2022.
[28] Our World in Data, 'Share of people vaccinated against COVID-19', *Our World in Data,* 30 June 2021, accessed 17 August 2022.

A significant focus on logistics and delivery through the establishment of National COVID Vaccine Taskforce (NCVTF) and Operation COVID Shield meant that Australia was able to achieve very high rates of vaccination once sufficient vaccines were available (see Figure 6).

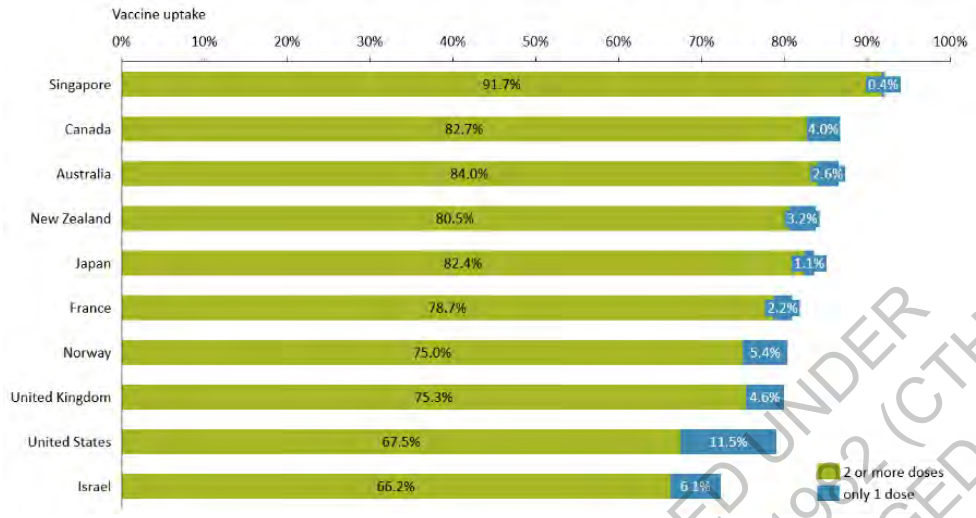
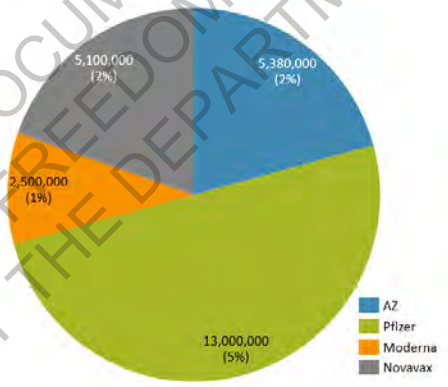


Figure 6: People vaccinated Against COVID-19 by country at 2 September 2022.[29]

A portfolio approach ensured that Australia had several 'shots on goal' at a time when it was necessary to enter into commitments ensuring adequate supply, with Advance Purchase Agreements (APAs) signed with five vaccine manufacturers: AstraZeneca, University of Queensland/Sequirus (later cancelled), Pfizer, Moderna, and Novavax (see Figure 7).

Pfizer was the first vaccine distributed in Australia and became the most widely available vaccine after AstraZeneca was restricted following concerns over potential side effects, particularly for in ensuring ongoing protection for lives and livelihoods patients.

The most administered vaccine in Australia has been the Pfizer vaccine (42 million doses, 69%), followed by AstraZeneca (13 million doses, 22%), then Moderna (5 million doses, 8%), and lastly Novavax (180k doses, <1%) (see Figure 8).



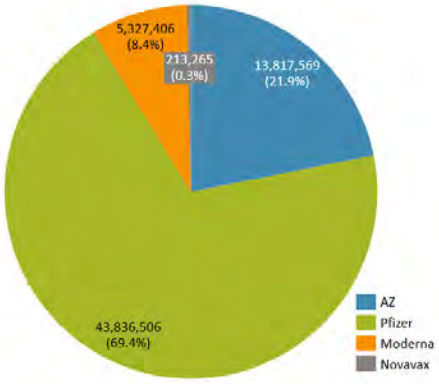


Figure 7: (left) Australian doses purchased by vaccine type.[30]
Figure 8: (right) Australian doses administered by vaccine type.[31]

[29] Our World in Data, 'Share of people vaccinated against COVID-19', *Our World in Data,* 2 September 2022, accessed 6 September 2022.
[30] Provided by Department of Health and Aged Care, data as at 2 September 2022.
[31] Provided by Department of Health and Aged Care, data as at September 2022.

Vaccinations were not available to those aged 16 or younger in Australia until 27 August 2021 and are still not available or recommended for this cohort in all countries. This means international data to compare vaccinate rates of children and adolescents are not readily available. Australia's performance in vaccinating paediatric cohorts is comparable to international rates except for Singapore which has significantly outperformed relative to other countries. Australia has achieved two dose vaccine coverage of 40.6% for children aged 5 to 11 years of age (see Figure 9).

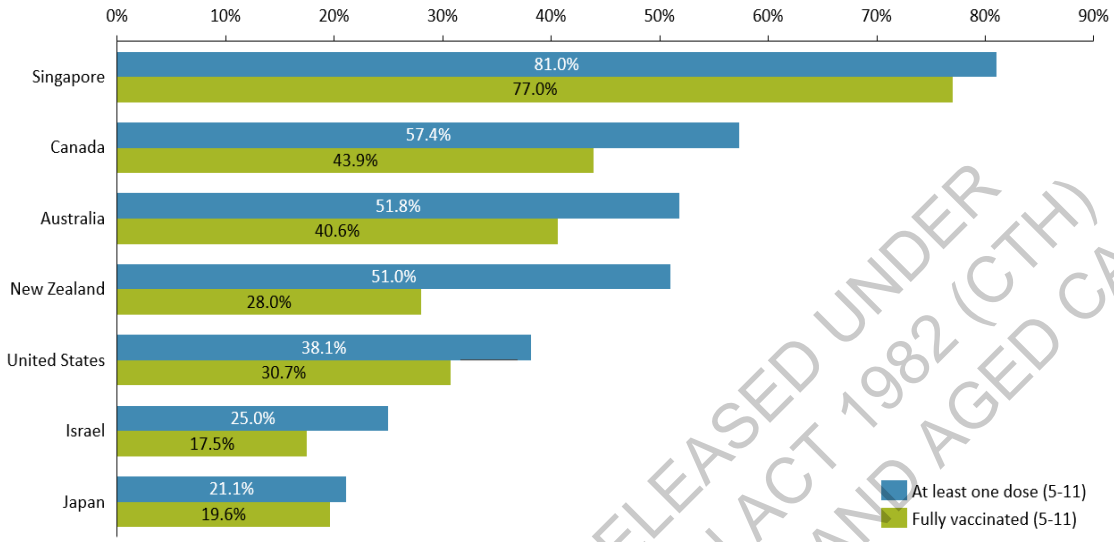


Figure 9: Vaccination of age 5 to 11 cohort by country.[32]

Due to the reduced efficacy of the existing vaccine products against the newer variants of SARS-CoV-2, some countries recommend a fourth dose of eligible vaccines, especially to older people.

In Australia, expanded eligibility for a fourth dose of a COVID-19 vaccine was approved in July 2022 and includes all individuals aged 30 and over in anticipation of an increase in immune response against new variants as was observed following the first booster (see Figure 10).[33]

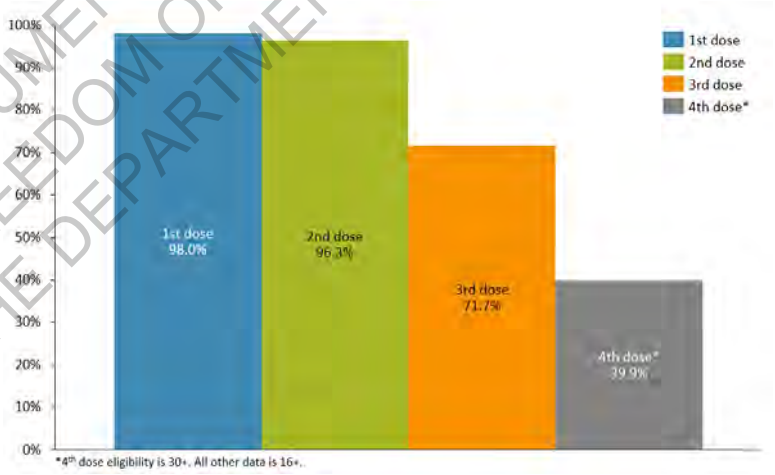


Figure 10: Australian vaccine coverage by dose number (age 16+).[34]

[32] European Centre for Disease Prevention and Control, 'COVID-19 Vaccine Tracker', *European Centre for Disease Prevention and Control,* accessed 03 August 2022.
[33] Australian Government, 'ATAGI updated recommendations for a winter dose of COVID-19 vaccine' [media release], *Department of Health and Aged Care*, 07 July 2022, accessed 09 August 2022.
[34] Provided by Department of Health and Aged Care, data as at 2 September 2022.

While long term data on increased protection offered by a fourth vaccine dose are limited, initial studies show that the short-term effect of a fourth dose does increase protection against the Delta and Omicron variants relative to the waning protection of a third dose after five months.[35] See Attachment 4.

While Australia has had early success with managing the pandemic, further emergence of new variants and management of the vaccination rollout has seen waning performance in comparison to other countries. Australia currently has the second lowest rate of booster uptake among comparator countries (see Figure 11).

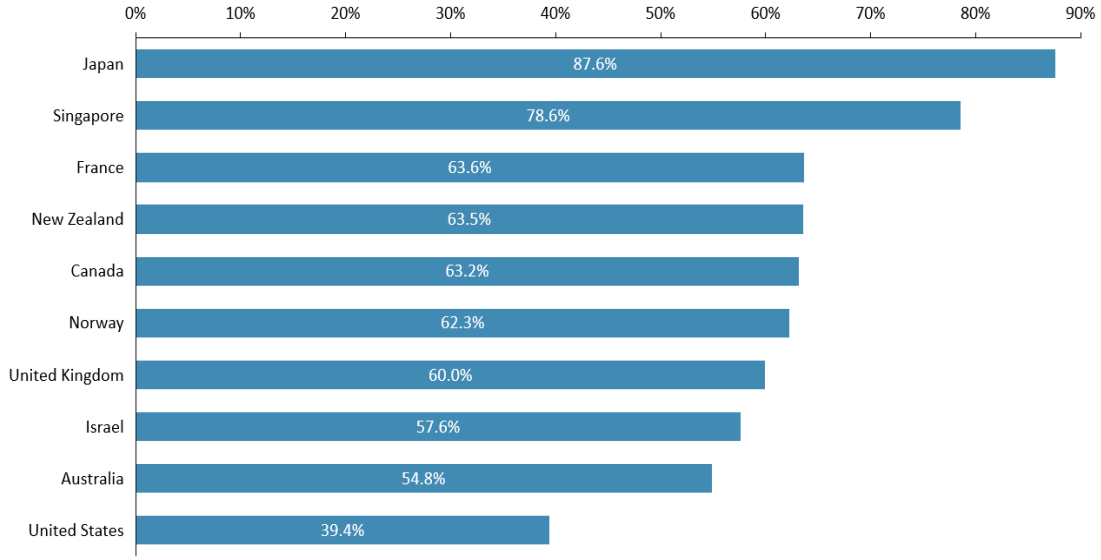


Figure 11: COVID-19 vaccine boosters administered per 100 people by country.[36]

Australia has been successful at achieving high rates of primary course vaccination and maintaining a low death rate, but relative performance is beginning to wane.

Reasons for this slower uptake include a lack of awareness of the importance of boosters, inconsistent messaging from health authorities, and hesitancy by some members of the public. In Australia, the third dose of the COVID-19 vaccination program was not made available to the general public until 8 November 2021.[37] Following the emergence of the Omicron variant, the booster program was again expanded to reduce the recommending timing for a booster dose from six months to four months following a second dose in December 2021, and to three months in January 2022.[38] In France, the booster program began in September 2021 and expanded eligibility in November 2021. Singapore also introduced their vaccination booster program in September 2021 and expanded eligibility to those aged 30 and above in October 2021.[39]

[35] G Regev-Yochay et al., '4th Dose COVID mRNA Vaccines Immunogenicity & Efficacy Against Omicron VOC', *medRxiv*. 15 February 2022, accessed 09 August 2022

[36] Our World in Data, 'COVID-19 vaccine boosters administered per 100 people, Aug 14, 2022', *Our World in Data,* accessed 14 August 2022.

[37] Australian Government, *Start of COVID-19 booster vaccination program* [media release], Department of Health and Aged Care, 08 November 2021, accessed 16 August 2022.

[38] Australian Government, *Four million additional Australians eligible for their booster dose* [media release], Department of Health and Aged Care, 31 January 2022, accessed 16 August 2022.

[39] Singapore Government, *Updates on expanded vaccination programme, facilitating our vaccination booster programme* [media release], Singapore Ministry of Health, 30 October 2021, accessed 16 August 2022.

***Recommendation 1**: Public health campaigns designed to encourage sustained booster uptake for those that will benefit should be developed and delivered during 2023/24 to increase coverage.*

In Australia, there are several treatment options provisionally approved by the Therapeutic Goods Administration (TGA) for use, including five anti-SARS-CoV-2 monoclonal antibody treatments (Evusheld, Regkirona (no supply in Australia), Actemra, Ronapreve, Xevudy) and three antiviral agents (Veklury, Lagevrio and Paxlovid). An overview of the TGA approved indications for use, clinical efficacy against variants of concern, real-world effectiveness, safety, supply, distribution and key ongoing clinical trials is outlined at Attachment 5.

4 Regulation of vaccines and treatments

The TGA is responsible for the regulation of therapeutic goods in Australia. The TGA played an important role throughout the pandemic in ensuring safe and timely access to vaccines and treatments. Developers and manufacturers moved at speed to develop products, undertake clinical trials, and register their products in multiple countries, placing a significant burden on regulatory agencies.

There was little or no time lag between submission to Australia compared with larger markets such as the US and Europe. Further information regarding the role of the TGA, its approval processes and activities during the pandemic is available at Attachment 6.

4.1 Approval of vaccines and treatments

The TGA approves inclusion of vaccines and treatments on the Australian Register of Therapeutic Goods (ARTG) via the provisional registration pathway (see Figure 12). It is also able to utilise emergency use provisions under Section 18A of the *Therapeutic Goods Act 1989*.[40]

Figure 12: Australian TGA provisional registration pathway.

Emergency use provisions were enacted on 2 April 2020 to allow medicines containing remdesivir, lopinavir and ritonavir, and hydroxychloroquine or chloroquine to be supplied in Australia without being registered. The exemptions were subject to the condition that the medicine must only be supplied in Australia for the prevention, treatment, or alleviation of COVID-19 under contract with, or by prior written arrangement with, the Australian Government Department of Health. The exemption provisions ceased on 31 January 2021.

Unlike the Food and Drug Administration (FDA) in the US, the TGA did not utilise emergency use provisions for the evaluation and approval of vaccines or other treatments. A provisional registration process, underpinned by a 'rolling review', enabled a timely and effective response.

There is no provision under law for TGA emergency use provisions to require a sponsor to submit data. Consequently, adjustments to the registration processes for COVID-19 products were made including:

[40] *Therapeutic Goods Act 1989*, Section 18A.

- Enabling multiple products for the same condition (COVID-19) to be eligible for provisional designation and approval;
- accepting rolling data;
- introducing various conditions of registration and post-approval commitments;
- introducing the ability to make multiple regulatory decisions within one application;
- accepting use of international labels; and
- organising *ad-hoc* meetings of the Advisory Committee on Vaccines (ACV) or Advisory Committee on Medicines (ACM).

To accommodate these adjustments, changes were agreed and implemented to various legislative instruments, including but not limited to the *Therapeutic Goods Act 1989*, *Therapeutic Goods Regulations 1990* and the Poisons Standard.

The elapsed approval timeframes achieved by the TGA were comparable with those of the FDA and European Union (EU) (see Attachment 7). In some cases, the TGA was one of the first regulators globally to approve a product. In some instances, sponsors did not prioritise the submission of regulatory approvals in the smaller Australian market until larger regulators, such as the FDA, had provided feedback on relevant applications.

The TGA collaborated extensively with other regulators. Despite country specific issues, similar challenges included dossier data gaps, differences in international labels, and transportation of vaccines at -80°C. Global collaboration included information exchange at EU discussions on safety, efficacy, and quality of vaccines, and shared evaluations with the Access Consortium (a coalition of regulatory agencies from Australia, Canada, Singapore, Switzerland, and the UK).[41]

Feedback from the sponsors of vaccines and treatments indicate a desire to retain some of the changes that were made. For example, changes to labelling requirements including acceptance of international labels and the use of QR codes to provide product information were positively received and lessened the regulatory burden of supplying therapeutic goods in Australia. Sponsors also noted the significant efforts required to make minor updates to product dossiers across multiple countries.

Where appropriate, Australia should continue to look for opportunities to ensure consistency with other global regulators. Consideration should be given to permanent implementation of changes made during the pandemic which ease regulatory burden and do not impact public safety.

4.2 Post market surveillance and safety

The TGA is also responsible for monitoring the safety of vaccines and treatments as part of its post market surveillance and consumer safety functions. Over the course of the pandemic, the TGA has received and responded to over 200,000 consumer queries relating to COVID-19 vaccines and treatments. The TGA operates on a cost recovery model which has created a significant funding shortfall in relation to post-market surveillance and consumer safety activities. The average fee per product collected to fund these activities is $17,000, whereas the TGA has spent over $5 million on COVID vaccine safety activities.

[41] TGA, 'Australia-Canada-Singapore-Switzerland-United Kingdom (Access) Consortium', *Therapeutic Goods Administration,* 14 December 2021, accessed 24 August 2022.

Funding available to the TGA should enable it to continue its important work regarding pharmacovigilance and consumer safety.

5 Policies, decision-making and advisory mechanisms

Rapid decision-making was required by governments around the world to respond to high infection levels and strain on hospital systems (first seen in Italy in March 2020). Existing decision-making systems and processes were disrupted as a consequence of the emerging crisis. In some countries, existing reserve powers including in respect of vaccine/therapeutic manufacturing, were invoked. Export restrictions were also imposed and shortages of critical medicines and supplies became a significant focus for national governments.

In Australia, a National Cabinet was announced on 13 March 2020 to coordinate responses across the states and territories.

Public health measures were largely imposed on a state and territory basis with the Australian Health Protectional Principal Committee (AHPPC) as a key source of advice to National Cabinet in respect of shared/agreed responsibilities.

Procurement of vaccines and treatments was undertaken nationally with delivery and administration via multiple channels. Decisions on vaccine and treatment purchases were made by the federal cabinet on the advice of the Science and Industry Technical Advisory Group (SITAG).

In addition to advice on the implementation of public health measures designed to limit the spread of infection, decision-makers took broad advice from several expert bodies on the handling of the acute phase of the pandemic. This advice was a crucial element in the *ad hoc* framework for decisions-making including purchase of vaccines and therapeutics plus eligibility and treatment criteria needed during the acute phase of the pandemic.

5.1 Decision-making in a pandemic environment

In the 'pre-COVID' context, the distinction between the role of individual decision-makers in respect of vaccines was clear.

The TGA licences products for use (including any restrictions). Governments decide what to publicly fund/procure based on advice from the Australian Technical Advisory Group on Immunisation (ATAGI), the Pharmaceutical Benefits Advisory Committee (PBAC), or state-based mechanisms. Decisions on how to finance public access to the products (usually via the National Immunisation Program (NIP) or the Pharmaceutical Benefits Scheme (PBS)) follows. Clinicians decide what to prescribe or administer to patients using clinical guidance as appropriate.

Decisions about the procurement of vaccines and treatments by governments are made in a context where evidence, value for money, and distribution mechanisms are all considered. These mechanisms are well understood, and processes and procedures are well practised. There is clear understanding of policy objectives, and the likely levels of eligibility and demand are factored into purchasing decision.

Distribution is factored into program design with prescribed products distributed mainly via hospitals, pharmacy, and, in some cases, doctors' surgeries or workplaces. Specific programs are designed to achieve objectives, particularly public health benefits, such as childhood immunisation or adult influenza vaccination for vulnerable populations. Communication to the public about availability and benefit of vaccines is designed to drive uptake.

While government subsidies for vaccines/therapeutics are decided on a cost-benefit basis, the total burden of disease in the community is determined by the total uptake of the product (together with the effectiveness of public health measures).

Decision-making in respect of the NIP reflects these roles and is driven by clear policy objectives, known eligibility, ability to forecast likely demand (based on previous uptake), and established distribution systems through states and territories and community wholesalers (see Figure 13).

Figure 13: Australian health procurement decision-making process (normal state).

While a product may not be subsidised for provision to an individual, a clinician can still prescribe products if they believe it is in the best interest of their patient. These products are dispensed as a private script. To fulfil this need, there is a significant private market for procurement of vaccines, including for influenza vaccines (see Figure 14).

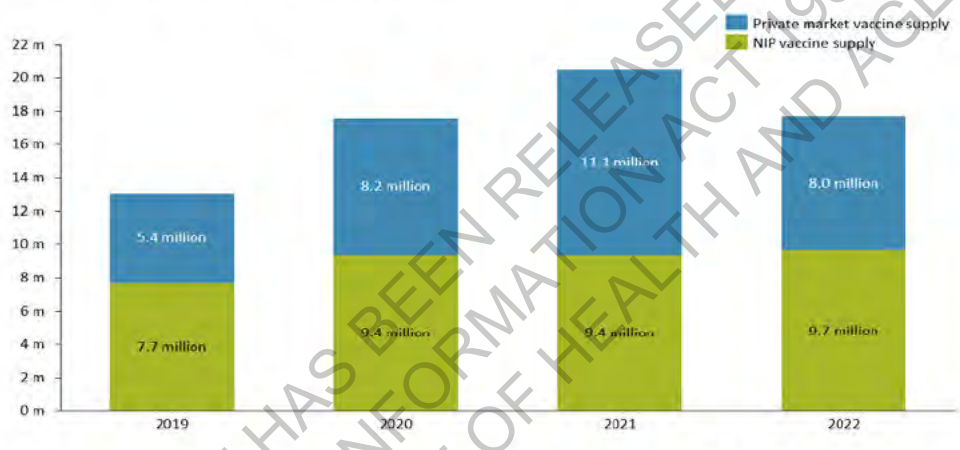


Figure 14: Influenza vaccines cleared by the TGA from 2015 to 2022.[42]

This 'usual' approach to provision of publicly funded vaccines has been disrupted during the pandemic. All COVID-19 products (vaccines and therapeutics) are publicly funded, there is no private market, and eligibility criteria are absolute in determining access. As such, total reduction in the burden of disease due to the use of vaccines/treatments is defined only by publicly funded vaccines and treatments and public health measures.

The various trade-offs required to achieve desired policy settings are inherent in any decision-making process (see Figure 15).

Pandemic decision-making processes were iterative due to multiple factors influencing each stage. For example, procurement decisions were made prior to or in tandem with policy development due to the significant global demand for COVID-19 products. To secure supply in a constrained global market where success/availability was not certain, early APAs were needed to secure access to successful products. There were significant unknowns regarding virus behaviour, whether vaccines or treatments would be effective, and the number of vaccines and treatments required for each cohort.

[42] Provided by Therapeutic Goods Administration, data as at 21 August 2022.

Eligibility decisions for the provision of vaccines and treatments were made in a rolling manner which impacted public messaging and uptake. While ATAGI has continued to provide advice about the use of vaccines, this advice has changed over time and does not provide a firm foundation for procurement decisions (e.g., original advice about boosters required significantly fewer vaccines then now implied by current advice).

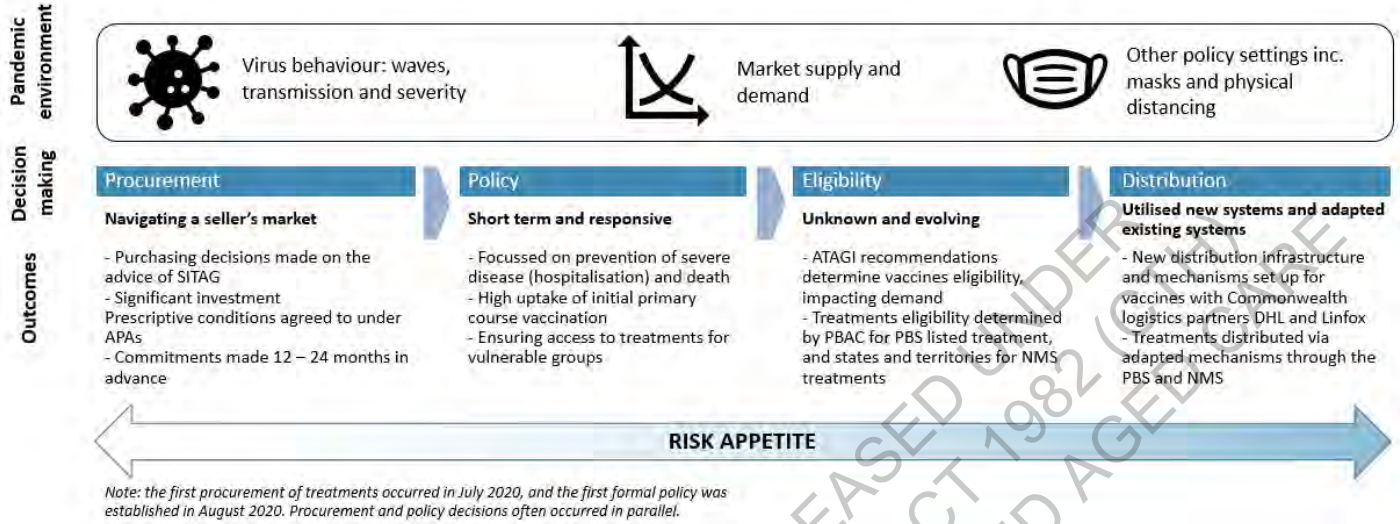


Figure 15: Australian health procurement decision-making process (pandemic state)

The government decided existing distribution networks through the NIP, Pharmaceutical Benefits Scheme (PBS), and National Medical Stockpile (NMS) were not suitable for the COVID-19 context. New distribution channels for vaccines were established to meet requirements around cold chain infrastructure, temperature monitoring, stock and wastage reporting, and scalability. For treatments, the PBS and NMS were utilised for distribution but required the implementation of *ad hoc* pandemic arrangements.

5.2 Policy settings

Current policy objectives were established in late 2020. Key components were to:

- Provide the widest protection through vaccines to an immunologically naïve population;
- Offer treatments, when available, to mitigate the effects of infection; and
- Prevent severe disease and death.

Protection of lives and livelihoods was the key goal.

To achieve these objectives and based on input from key advisors/advisory structures agreed elements of the policy approach were:

- A whole of population approach to the administration of vaccines;
- A portfolio approach to vaccine and treatment procurement to ensure access/redundancy, at the time, due to uncertainty of success, timelines of delivery and likely global shortages; and
- An emphasis on domestic manufacture where possible.

These settings remain largely in place today and are contained in:

- The Vaccine and Treatment Strategy released on 19 August 2020, which recognised existing architecture of NIP and PBAC/PBS was not fit for purpose in this emergency context,

announced APAs to direct purchase of vaccines and treatments and nominates an expanded role for ATAGI to provide advice on vaccinations;[43]

- The Commonwealth Procurement Rules exemption for procurement of COVID-19 vaccines and treatments on 19 August 2020;
- SITAG advice which recommended portfolio approach to vaccine procurement on 9 September 2020;
- ATAGI advice provided on 23 September 2020 recommended two doses for all adults and included groups which required priority vaccination;
- The Australian COVID-19 Vaccination Policy endorsed by National Cabinet on 13 November 2020;[44]
- Australia's COVID-19 Vaccine National Rollout Strategy released on 7 January 2021;[45] and
- SITAG provided further advice diverse portfolio approach should be adopted for procurement of treatments 6 September 2021.

This broad framework does not include a strategy for the distribution of treatments as they were not widely available in 2020. A systems-based understanding of distribution and delivery arrangements is important to ensure access by patients who are eligible and in need of treatment. Similarly, transparency and communication with industry and sponsors, which some have commented is lacking, will help ensure widest possible and timely access to effective products.

It is noteworthy that the objective of domestic manufacturing of vaccines has been a priority for many years. CSL was originally founded as a government enterprise which delivered on shore manufacturing, including of vaccines. Vaccines manufactured at CSL during 2021 were crucial to the overall adequacy of supply during the early part of the rollout. These vaccines were targeted to older people with imported vaccines being targeted to largely younger cohorts.

A timeline of key policy decisions is provided at Attachment 8.

The need to mitigate the effects of COVID-19 is likely to remain. However, policy settings have not been updated to take account of already widespread COVID-19 infections and associated high levels of hybrid immunity, the possibility of future waves and variants, and developments in vaccine and therapeutic science and manufacturing. A portfolio approach and potentially redundancy will be needed to ensure access.

Australia is no longer in the grip of the acute phase of the pandemic, but short and medium-term prospects remain uncertain as ongoing waves of the virus continue to disrupt lives and livelihoods. It is not yet possible to manage COVID-19 in a similar way to endemic respiratory viruses.

[43] Australian Government, 'Australia's COVID-19 Vaccine and Treatment Strategy', *Department of Health and Aged Care*, 19 August 2020, accessed 29 August 2022.
[44] Australian Government, 'COVID-19 Vaccination Policy endorsement', *Department of Health and Aged Care*, 13 November 2020, accessed 28 August 2022.
[45] Australian Government, 'COVID-19 vaccination – Australia's COVID-19 vaccine national roll-out strategy', *Department of Health and Aged Care*, 07 January 2021, accessed 28 August 2022.

This context continues to present real challenges in decision-making in respect of procurement of, eligibility for, and distribution of both vaccines and treatments. Supply chain issues remain with potential shocks or spikes in demand hard to estimate.

In the period of transition to 'COVID-stable', procurement decisions must be made in the context of significant unknowns – including virus behaviour and ongoing population eligibility/demand for vaccines. Demand will be largely a function of waning immunity, efficacy of available vaccines, eligibility, and the risk of severe disease and death. Continued emphasis on the benefits of vaccination, particularly to people most at risk, will be important in ensuring high levels of protection.

Partially or fully mitigating the downside risk of multiple waves or variants with increased severity will require investment in additional vaccines and treatments, some of which may be wasted.

Australia's risk appetite will frame the management of these issues for the next 12 to 24 months. Our appetite for shortages, events which cause exhaustion of stock (stock-outs), or failure to access supply at short notice are crucial to COVID-19 management, particularly in the event of a new variant of concern. Similarly, the role of targeted access limited by (under) supply requires further consideration.

Usual health technology and pharmaceutical assessments are well established but have not been broadly applicable during the early stages of the pandemic due to global shortages. The usual decision-making processes have been disrupted. In this context, there is a contradiction between the end point of 'preventing severe disease and death' (which should remain the overarching objective and basis for targeting in the event of supply shortage) and more permissive access settings enabled by supply.

In the short-term, wider eligibility for some treatments should be considered where there are stocks available, there is evidence of efficacy, safety, and broader economic and societal benefits (such as workforce availability). This is particularly the case where there is no significant private market to help limit the burden of disease.

Despite still transitioning to a 'COVID-stable' context, emergency and *ad hoc* settings should be transitioned to new, fit for purpose structures and processes. Planning should also commence for the eventual transition to the management of COVID-19 as an endemic respiratory virus.

A clear statement of updated policy objectives for the ongoing management of COVID-19 would assist decision-making in respect of purchasing, eligibility, and in a clinical context. This should take account of the disruption experienced over the last two and a half years, the ongoing need to manage new waves of disease, existing stocks of vaccines and treatments (particularly where there are sunk costs), and public health, economic and wider objectives including mental health, social, and education outcomes.

Recommendation 2: *A clear, updated, policy framework including objectives for the management of COVID-19 should be developed to inform decision-making, purchasing, clinical decision-making and resource allocation. A statement of risk appetite should form a part of this framework.*

5.3 Governance, regulatory and advisory bodies

Australia's existing policy framework for access, supply, and procurement of vaccines and therapeutics, while effective for pre-pandemic business as usual, were not well suited to pandemic conditions.

A pandemic environment requires speed and agility, the capacity to scale, and mechanisms to address uncertainty and mismatches between supply and demand. Novel approaches to procurement and distribution of vaccines and treatments are also required.

During the early stages of the COVID-19 pandemic new approaches were needed. This included changes to advisory mechanisms to assist decision-making on:

- what vaccines and treatments should be procured; and
- the use of these vaccines and treatments.

Several advisory committees had their remit extended and more were created to extend the nature and scale of advice available to decision-makers.

All committees have provided advice, often in an environment of uncertainty and under considerable time pressure, to assist in decision-making including by clinicians. In some instances, members of previously unknown committees have become quasi-public figures and been subjected to considerable pressure in the conduct of their roles. In many instances, their advice has been provided as an adjunct to full time academic or clinical roles.

In view of the current phase of the pandemic and changed circumstances, it is timely to consider whether existing committee structures and remits remain appropriate and fit for purpose.

5.3.1 Australian Health Protection Principal Committee

The Australian Health Protection Principal Committee (AHPPC) is the key decision-making committee for health emergencies relating to infectious diseases, the environment, and human and man-made natural disasters. It is comprised of all state and territory Chief Health Officers and is chaired by the Australian Chief Medical Officer. The Committee works with states and territories to develop and adopt national health protection policies, guidelines, standards, and to align plans. The AHPPC oversees five standing committees and one advisory group.[46]

AHPPC is a long-standing committee with an agreed and well understood role. While relevant to the distribution of both vaccines and therapeutics at the state level, their focus necessarily shifts with the priorities of the moment. They will continue to play a key role in decision-making, advice and liaison in the short term as the pandemic transitions to a more stable and predictable state. See Attachment 9.

5.3.2 Science and Industry Technical Advisory Group

Decisions to invest in COVID-19 vaccines and treatments are supported by advice from a combination of scientific, medical, and industry development experts. The COVID-19 Vaccines and Treatments for Australia Science and Industry Technical Advisory Group (SITAG), chaired by the Chief Medical Officer, was established in August 2020. It first met on 16 August 2020. Membership includes scientists, biotechnology, and pharmaceutical experts. See Attachment 10.

The SITAG meets as required by the Department and/or the Minister to provide advice on the purchase of COVID-19 vaccines and treatments based on current data and epidemiology. Current

[46] Department of Health and Aged Care, Australian Health Protection Principal Committee (AHPPC) [website], n.d., accessed 1 September 2022.

investments are subject to the advice of the SITAG, including assessment of clinical evidence, portfolio diversification and risk.

The SITAG provides advice on:

- the safety and effectiveness of potential COVID-19 vaccines, tests, and treatments;
- purchasing COVID-19 vaccines, tests, and treatments for Australia;
- the options available for manufacturing and packaging COVID-19 vaccines and treatments in Australia;
- distribution and logistics associated with potential COVID-19 vaccines; and
- other technical matters related to COVID-19 vaccines and treatments.

Summaries of the SITAG recommendations and considerations are now available publicly.[47]

s47E, s34(3)

The SITAG members are appointed by the Minister. Current members have been invited to extend their appointment to 31 December 2022.

Over the course of the pandemic, the SITAG has played a key role in ensuring that procurement and supply decisions were made in a timely manner to secure access. The importance of early advice to purchase vaccines and therapeutics, often prior to registration, is now well understood, particularly in an environment of significant global demand.

A critical capability that the SITAG members bring to the 'advice ecosystem' is an understanding of research, drug development and manufacturing, global supply chains, and the importance of ongoing engagement with relevant companies to ensure priority access for Australia. This represents a new and important perspective which is not available through other committees or within the Department.

Deep and productive relationships with an understanding of research, development and manufacturing are critical to decision-making and access. These perspectives should continue to inform decision-making going forward, noting the need to manage any potential conflicts of interest, including commercial interests.

5.3.3 Australian Technical Advisory Group on Immunisation

The Australian Technical Advisory Group on Immunisation (ATAGI) was established in 1998 to advise the Minister for Health on the medical administration of vaccines available in Australia. The ATAGI advises the Minister for Health on vaccines for inclusion on the NIP and other immunisation issues and provides advice to research organisations on current and future immunisation research.

The ATAGI also provides industry sponsors with pre-submission advice for potential submissions to the PBAC on vaccine effectiveness and use in Australia. Advice from the ATAGI must be sought prior to a sponsor making a submission to the PBAC. Taking into consideration commercial and in confidence nature of the information discussed by the ATAGI, the advice provided is not publicly available and as such is mainly considered by the Minister as part of their decision-making. Outcome statements were issued intermittently.

[47] Australian Government, 'The COVID-19 Vaccines and Treatments for Australia – Science and Industry Technical Advisory Group summaries', *Department of Health and Aged Care*, 17 August 2022, accessed 28 August 2022.

The ATAGI commenced discussions on COVID-19 vaccines in February 2020 and in August 2020 established an ATAGI COVID-19 Working Group. The working group comprised the ATAGI executive team and three subgroups: technical and clinical advice; immunisation landscape; and safety and monitoring. See Attachment 11.

Early in the pandemic, government decided that, *inter alia,* all advice from the ATAGI would be accepted. Further, that the outcomes of the ATAGI deliberations would be made public. This has led to representation of the outputs of the ATAGI as decisions and caused widespread confusion about responsibility for decision-making.

The ATAGI's initial advice focussed on which groups should be prioritised for early vaccine access. This was in a context where supply shortages meant that priority, rightly, needed to be given to those groups most at risk of poor outcomes from contracting COVID-19.

The ATAGI has continued to provide updated advice on vaccination as new vaccines and formulations have been approved by the TGA, new cohorts have become eligible, and adverse medical events were reported.

More recently, available supply has exceeded demand fed by narrowly framed eligibility. Procurement decisions, including the volume of product purchased, preceded eligibility decisions. The portfolio approach to procurement, which has ensured supply, has meant there is a mismatch between supply and eligibility criteria as advised by ATAGI.

Further, the ATAGI recommendations for use have often been framed more narrowly than the regulatory approvals provided by TGA. Eligibility criteria have been changed based on advisory committee advice (often characterised as decisions) about safety and efficacy. Subsequently, there has been confusion about the roles of the TGA and the ATAGI with respect to post market safety surveillance and authority to restrict access to products outside of a supply constrained context.

The ATAGI advice, which is released publicly, is often treated as prescriptive and rules based. The timeliness of this advice has also been questioned.

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Recommendation 3: *Advisory structures should be streamlined, and advice should be integrated to enable actual decision-makers to undertake their role. The role of the decision-makers and advisors should be clarified. Reasons for decisions should be evidenced including indicating where they are based on judgment. Care should be taken to prevent confusion at the clinical level about who is eligible to receive vaccines/treatments and recommendations for use including in respect of target populations.*

6 Access to COVID-19 Vaccines

Work commenced on vaccine development as soon as the SARS-CoV-2 genetic sequence was available in early January 2020. In what can only be described as an unprecedented global race, many parties were engaged in research and development activity around the world utilising a mix of technologies, including leveraging earlier work on SARS. The objective was to develop a successful vaccine as fast as possible to reduce severe disease and death. There was no guarantee of success.

Progress and early clinical results were scrutinised closely and as companies working on vaccines began to report early success in clinical trials, many high-income countries struck procurement contracts for fulfilment in the event of success. This included Pfizer executing agreements with the UK on 20 July 2020, US on 22 July 2020, and Japan on 31 July 2020.

Successful COVID-19 vaccines first became available in late 2020.

Early agreements enabled the UK to begin their vaccine rollout on 8 December 2020,[49] while the US began their vaccination program on 14 December 2020. [50]

In 2020 and 2021, global vaccine supply was challenged, including with shortages of raw materials (namely lipid nanoparticles used to deliver RNA into cells), delays to upscaling production, and localised lockdowns in vaccine producing countries. This led to countries with local manufacturing capacity, such as the US and the UK, prioritising domestic shipments of vaccines.

Predictably, global demand was much greater than available supply at the beginning of the pandemic. Early deliveries prioritised pre-purchasing agreements except where export restrictions delayed availability. The domestic manufacturing capability of other countries, such as the US, UK, and Japan, resulted in an expedited vaccine rollout in comparison to Australia, which was partially dependant on overseas supply.

These countries were able to leverage pre-existing pharmaceutical development ecosystems and onshore ability to mass produce vaccinations which facilitated priority access. Australia had some

[49] United Kingdom Government, *UK marks one year since deploying world's first COVID-19 vaccine* [media release], Department of Health and Social Care, 08 December 2021, accessed 30 August 2022.
[50] CDC, 'CDC Museum COVID-19 Timeline', *CDC,* 16 August 2022, accessed 30 August 2022.

pre-existing infrastructure for vaccine production and CSL was contracted to produce the AstraZeneca viral vector-based vaccines.

When ATAGI updated advice restricting supply of the AstraZeneca vaccine to specific age groups (initially to those over the age of 50 years, and then to those over 60 years) due to the rare side effect of Thrombosis with Thrombocytopenia Syndrome (TSS), eligibility for available vaccines was stratified by age in order to ensure coverage. There was no onshore production capacity available to fill the gap in supply. Subsequently (December 2021), the Australian Government in partnership with Moderna, announced that an mRNA facility would be built and operational in Victoria from 2024, reducing the reliance on imported mRNA vaccines.[51]

Australia signed APAs with vaccine manufacturers later than other comparative countries which delayed the supply of vaccines and the speed of the rollout. While the US and the UK signed agreements with AstraZeneca in May 2020, Australia's first APAs were not announced until 9 September 2020 (AstraZeneca and University of Queensland). Australia then signed APAs with Novavax and Pfizer in early November, and Moderna in May 2021.

The EU imposed export restrictions on locally manufactured vaccines, beginning with Italy blocking a shipment of AstraZeneca vaccine to Australia in March 2021, due to a supply dispute between EU officials and AstraZeneca regarding exports of the vaccine to the UK.[52] The UK negotiated priority access for the AstraZeneca vaccines in return for investment in the vaccine candidate. These shortages of supply, amplified by vaccine nationalism, illustrated the challenges countries without local manufacturing capacity or purchasing power faced in securing vaccines in a timely manner.

Following the expansion of Australia's COVID-19 vaccine rollout, Australia overtook comparable countries to be a leader in primary course vaccination, with 83.89% of the eligible population having completed a primary dosage of a TGA approved vaccine as at 2 September 2022.[53]

As demand for vaccines grew, countries across the globe negotiated APAs to guarantee supply. High-income countries signed multiple APAs with manufacturers (an 'access premium') to ensure supply of different types of vaccines including mRNA, protein-based, and viral vector (see Table 1).

Country	AstraZeneca/ CSL	Moderna	Pfizer	Novavax	UQ/ Sequirus	Janssen	Sanofi/ GSK	Takeda	CureVac	Medicago	Serum Inst. Of India	Total
Type of vaccine	*Viral vector*	*mRNA*	*mRNA*	*Protein based*	*Protein based*	*Viral vector*	*Protein based*	*Protein based; mRNA*	*mRNA*	*Plant based virus-like particle*	*Protein based*	
Australia	✓	✓	✓	✓	✓							**5**
Canada	✓	✓	✓	✓		✓	✓			✓		**7**
UK	✓	✓	✓	✓		✓	✓		✓		✓	**8**
USA	✓	✓	✓	✓		✓	✓					**6**
New Zealand	✓		✓	✓								**3**
Japan	✓	✓	✓					✓				**4**
Israel	✓	✓	✓	✓								**4**

Note: Novavax licenced its technology to Takeda in response to demand in Japan.

Table 1: Vaccine types purchased by country.[54]

While some APAs did not result in delivery of doses due to failed clinical trials, countries were still able to ultimately procure up to six doses per eligible person. Adopting a portfolio and redundancy

[51] Premier of Victoria, *Victoria to Become Home Of mRNA Vaccine Manufacturing* [media release], Premier of Victoria, 14 December 2021, accessed 13 September 2022.
[52] ABC, 'Italy, EU refuse AstraZeneca request to ship 250,000 doses of vaccine to Australia', *ABC*, 5 March 2021, accessed 13 September 2022.
[53] Our World in Data, 'Share of people vaccinated against COVID-19', *Our World in Data,* 2 September 2022, accessed 6 September 2022.
[54] UNICEF, 'UNICEF COVID-19 Vaccine Market Dashboard', *UNICEF*, 29 July 2022, accessed 29 July 2022.

approach was a common strategy as initial information indicated only two doses were recommended for a primary course of COVID-19 vaccination (see Figure 16).

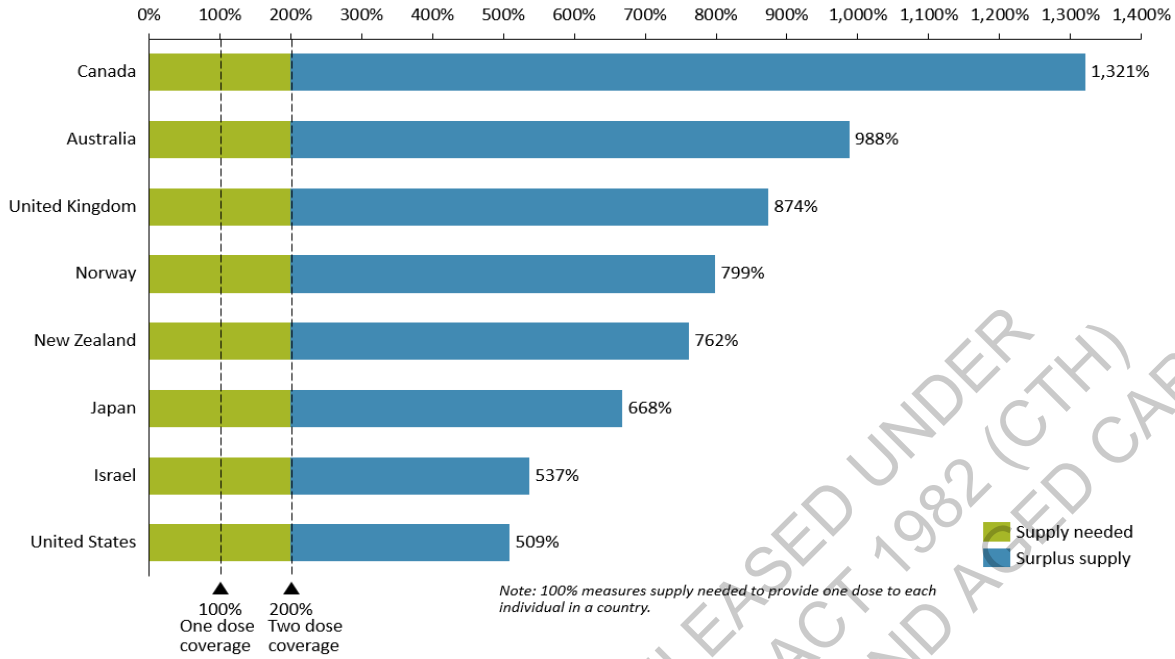

Figure 16: Doses purchased per capita by countries. Note: 100% represents the ability to provide primary course coverage to each individual in a country.[55]

Australia's procurement activities were consistent with other high-income countries. A portfolio and redundancy approach was adopted to mitigate risks and ensure adequate supply.

6.1 Procurement

On 19 August 2020, the Secretary of the Department, as the Accountable Authority, approved the application of the human health protection exemption under the Commonwealth Procurement Rules. This exempted procurement of COVID-19 vaccines and treatments from needing to comply with Division 1 and 2 of the Commonwealth Procurement Rules.

Australia signed APAs with AstraZeneca and the University of Queensland in September 2020, Pfizer in November 2020, and with Novavax in December 2020 for their vaccine candidates. These agreements ensured that Australia had access to at least 110 million potential vaccines, with subsequent agreements with Moderna and Pfizer bringing the number to 264.3 million doses.

Vaccine procurement decisions were required to be made many months in advance of possible supply in an extremely competitive and supply constrained environment (see Figure 17). The SITAG recommended a portfolio approach to ensure population wide coverage and mitigate against the risk of failed clinical trials, denial of regulatory approvals, and length of time to market. There were also significant unknowns including the number of doses required to maintain effective immunity against the virus and the extent to which the vaccines would prevent transmission, serious illness, and death against emerging variants.

[55] UNICEF, '[UNICEF COVID-19 Vaccine Market Dashboard]', *UNICEF*, 29 July 2022, accessed 29 July 2022.

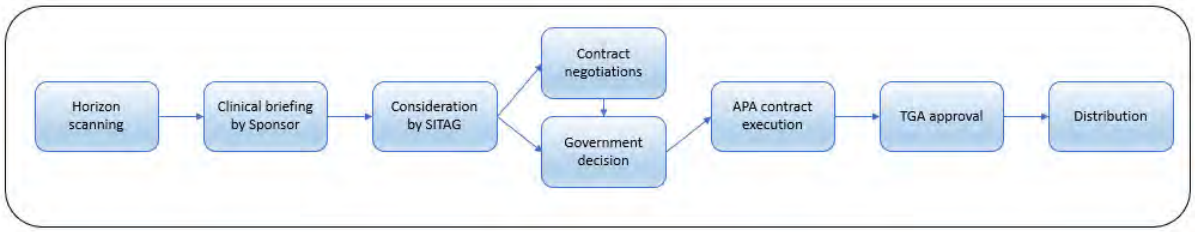

Figure 17: Procurement process for vaccines.[56]

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Early procurement of vaccines and treatments occurred in the context of uncertainty and a global vaccine shortage – a "sellers' market". Agreement to conditions not usually included in ordinary procurement contracts was necessary to secure commitments to supply.

Australia's foundational APAs are now nearing conclusion. The AstraZeneca APA has been completed and the last deliveries under the Moderna APA are expected by the end of 2022. The Novavax and Pfizer APAs extend into 2023 (see Table 2). As a consequence, new APAs giving effect to purchasing decisions will be needed.

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[56] Provided by Department of Health and Aged Care, data as at 3 August 2022.
[57] This attachment is protected under legal privilege.
[58] Provided by Department of Health and Aged Care, data as at 2 September 2022.

A portfolio approach will continue to be needed to mitigate the risk of supply shortage, delays, lack of success in clinical trials, manufacturing or regulatory failure.

Recommendation 4: *Procurement decisions should be made in the context of agreed policy objectives, risk appetite (the acceptability of failure to supply), knowledge/predictions in respect of the evolution of the virus, and supply constraints including knowledge of market behaviour.*

6.2 Distribution

Distribution of vaccines was a key challenge throughout the rollout. A Request for Proposal (RFP) was released on 5 November 2020 and an industry briefing was held on 11 November 2020. The proposals were assessed, taking into consideration end-to-end capability and capacity, ability to collaborate with the Department, data tracking and cyber security, and experience.

Through this process, Linfox and DHL were identified as Commonwealth logistics partners (see Table 3). The capacity to satisfy cold chain requirements for storage of vaccines was a key consideration in this determination. Pfizer vaccines are required to be stored at Ultra Low Temperatures (ULT) –90°C to –60°C and DHL was able to design and obtain the infrastructure required to meet this cold chain requirement. These conditions have evolved over time and at present, there is greater flexibility of storage both at frozen and thawed state.

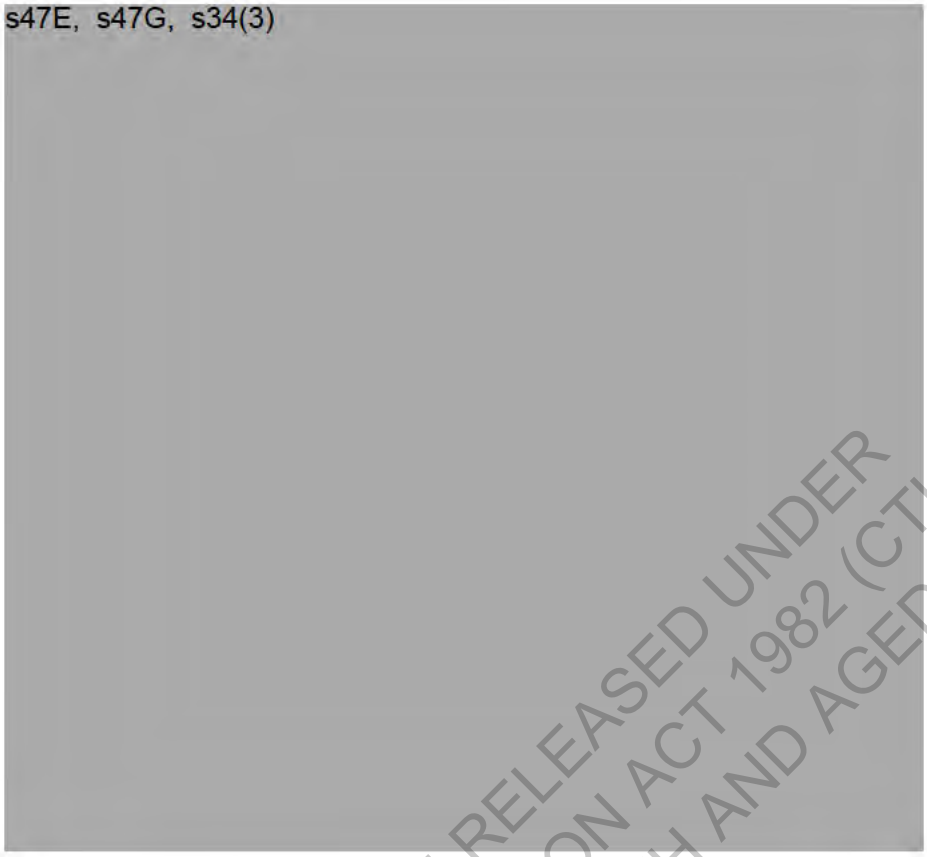
Vaccine	Vaccine Type	Storage Requirements
Moderna	mRNA	-50°C to -15°C
Novavax	Protein based	2°C to 8°C
Pfizer	mRNA	–90°C to –60°C
AstraZeneca	Viral vector	2°C to 8°C

Table 3: Storage conditions required for current vaccines.[59]

The RFP did not require tenderers to identify costs upfront due to the variable nature of the vaccine rollout. However, the top three tenderers were invited to respond to a hypothetical costing scenario to assess value for money considerations. Pricing schedules were agreed during the co-design and contract negotiation process. The pricing schedules contain a mixture of fixed and variable costs and have represented a significant investment in the vaccine rollout.

The current distribution model is split by vaccine type across each logistics provider (see Table 4).

[59] Provided by Department of Health and Aged Care, data as at 13 September 2022.



Most vaccines are manufactured offshore (with the exception of approximately 50 million doses of AstraZeneca which were manufactured at CSL) and were provided directly to delivery partners for distribution, following the appropriate clearance processes. Delivery partners maintain the appropriate cold chain infrastructure to ensure vaccines are stored in the required conditions, and temperature loggers are used to verify that appropriate conditions have been maintained throughout the distribution chain (see Figure 18). Any potential CCBs are reported and assessed for their impact on product quality and may result in doses being discarded. The Product Information (PI) for each vaccine provides for some minor controlled temperature excursions during the transportation process. See Attachment 13.

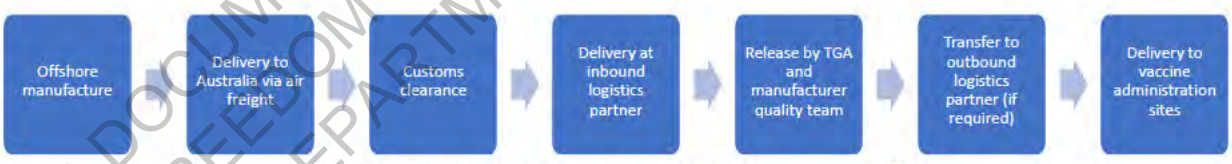


Figure 18: High level vaccine distribution process.[61]

Vaccine administrators are also provided with the consumables required to administer vaccines including needles, syringes, saline (for some formulations), sharps containers, and bandages. Consumables are procured via a consumables panel to obtain best price and are ordered and delivered via the same distribution channels as vaccines. These deliveries are not subject to the same reporting obligations in relation to cold chain breaches and wastage.

Delivery requirements for consumables are much less onerous than for vaccines. Current delivery arrangements should be reviewed to ensure value for money.

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[60] Provided by Department of Health and Aged Care, data as at 9 March 2022.
[61] Provided by Department of Health and Aged Care, data as at 2 September 2022.

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A bespoke ordering and reporting system, based on the Salesforce platform, COVID-19 Vaccine Administration System (CVAS) was commissioned to meet ordering and reporting requirements. CVAS is used by participating clinics for COVID-19 vaccine and ordering, supply, distribution, stock management, waste management, and redistribution. The system enables orders of inbound stock, movement between warehouses, and integrates with DHL and Linfox systems to ensure traceability of vaccines and consumables at each step of the distribution journey. The CVAS Vaccine and Consumables Ordering Process is included at Attachment 14.

The Vaccine Operations Centre (VOC) answers clinical, logistical, system, ordering and administration enquiries by phone and email, and refers issues for resolution through the program's Vaccine Issues Management System (VIMS). All enquiries and incidents are triaged and escalated where appropriate (see Attachment 14).

Within the VOC, the Clinical Team is specifically responsible for providing advice to vaccine administrators, including states and territories, on Vaccine Administration Errors (VAEs) and determining the outcome of Potential Cold-Chain Breaches (PCCBs). s47E, s47G, s34(3)

Current distribution arrangements utilise a weekly ordering system for states and territories and a fortnightly ordering system for all other vaccine administration sites. Fixed schedule ordering is suited to the management of significant numbers of deliveries and high demand but can result in significant wastage in periods of lower demand. As such, these attributes are less suited to the current context and will not be sustainable into the longer term. The benefits of adopting an on-demand distribution system are further explored in Section 8.1.

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Given the significant costs associated with distribution of vaccines, consideration should be given as to whether existing infrastructure (Community Service Obligation (CSO), states and current logistics partners) can be adapted to reduce outlays s47E, s47G, s34(3)

[62] Provided by Department of Health and Aged Care, data as at 2 September 2022.

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Recommendation 5: *Vaccine distribution arrangements should be reviewed in order to test value for money and to reduce wastage while ensuring timely access.*

6.3 Eligibility

Following provisional registration (approval) of a COVID-19 vaccine by the TGA, the Minister for Health determined eligibility to receive a vaccine based on the ATAGI advice and availability of vaccines. Over the course of the vaccine rollout there have been a number of occasions on which the ATAGI COVID-19 Working Group recommendations have been more narrowly framed than regulatory approvals, often as a response to supply shortages (earlier in the pandemic) or judgements about relative clinical differences (later in the pandemic as more vaccines became available). See Attachment 16.

The TGA's role is to consider the safety and efficacy of vaccines. As part of the provisional registration process (see Section 4.1), the TGA evaluates data provided from vaccine manufacturers to support use of the product within the specified cohorts. Manufacturers must submit additional applications for approval to include new cohorts or for use as a booster. Approved indications for use, contraindications and known side effects can be found in PI for each vaccine.

The ATAGI recommendations have considered various factors including:

- clinical information: recommendations are based on data provided by vaccine manufacturers and from independent studies to seek positive confirmation of a clinical benefit to a cohort;
- safety information: recommendations have considered the risk of adverse events or side effects based on data provided by vaccine manufacturers and from independent studies in each cohort;
- pre-existing health conditions: recommendations have considered the increased risk of serious illness or hospitalisation from COVID-19 in individuals with severe immunocompromise, complex health conditions, or disability, as well as older individuals;
- workforce requirements: recommendations have taken into consideration the risk of infection or of infecting others associated with working in critical jobs such as healthcare, aged care, or disability care; and
- vaccine supply: recommendations have taken into consideration the supply available to Australia to ensure that, when supply is limited, priority is determined based on sound clinical and ethical principles associated with the above factors.

Vaccine supply was a critical consideration in these eligibility decisions at the beginning of the pandemic. At this time, vaccine supply was low, and decisions were rightly made to prioritise cohorts who were considered most vulnerable to severe illness or hospitalisation from COVID-19 and critical workers (e.g., healthcare, aged care, and disability care workers). While recommendations were

updated as more information was available, the ATAGI initially provided advice on general principles to guide the prioritisation of target populations in a COVID-19 vaccination program (see Figure 20).[63]

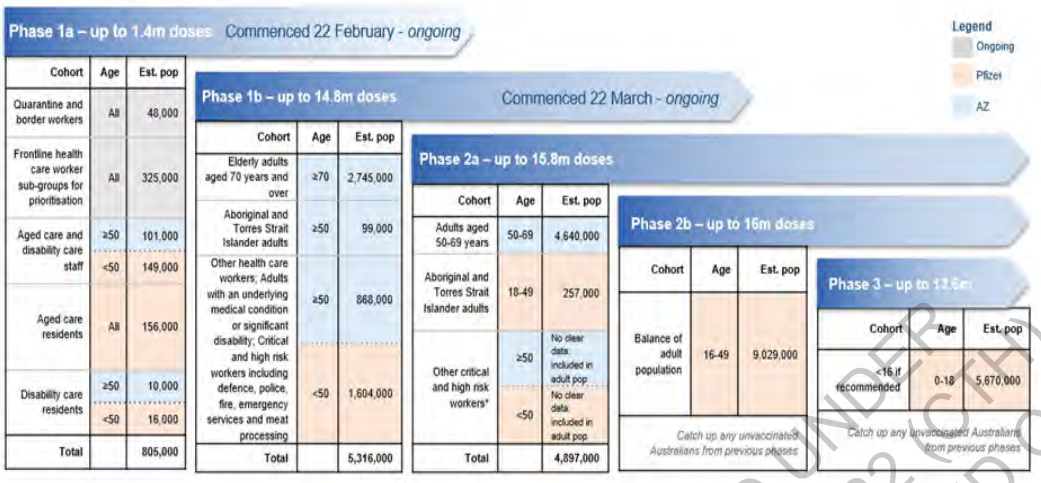

Figure 20: The phased approach to vaccine eligibility for various cohorts from the initial COVID-19 Vaccine National Rollout Strategy.[64]

This phased approach to vaccine eligibility was superseded as supply increased. Eligibility for each cohort has changed over the course of the pandemic in response to additional data from vaccine manufacturers or outcomes from other countries' vaccine programs.

Due to the complex and changing nature of eligibility over the course of the vaccine rollout, there have been reports of confusion and discontent from the public. This includes individuals being unaware of their eligibility for additional doses or certain vaccine products, as well as frustration from individuals who wish to receive additional doses but are currently not eligible. In addition, clinical guidance has, at times, been interpreted by vaccination providers as a strict eligibility requirement, rather than a recommendation to inform individual clinical judgement. This has resulted in some providers refusing access to patients who may benefit from vaccination.

Confusion between an approved indication for use (as determined by the TGA) and recommendations for use (based on advice from the ATAGI) is evident. Existing vaccine policy settings, which emphasise the goal of providing maximum protection to the entire public and maximising the use of available vaccine doses, can be seen as inconsistent with some current eligibility settings and some recommendations for use (see Section 5.2).

In order to maximise coverage and reduce confusion it is important to:

- *clarify who the key decision-maker on vaccine eligibility is and which bodies act in an advisory capacity;*
- *avoid complexity in eligibility criteria where there is no significant clinical difference between cohorts to ensure high levels of public awareness and vaccine uptake; and*
- *align key public messaging, public health goals, and high-level COVID-19 vaccine policy.*

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[63] ATAGI, 'ATAGI – Preliminary advice on general principles to guide the prioritisation of target populations in a COVID-19 vaccination program in Australia', *Department of Health and Aged Care,* 13 November 2020, accessed 16 August 2022.
[64] Provided by Department of Health and Aged Care, 3 August 2022.

6.4 Administration Channels

In Australia, COVID-19 vaccines have been made available through both state and territory hubs (mass vaccination sites) and through various other vaccination sites (collectively referred to as 'Primary Care' sites). In the context of the vaccine rollout, Primary Care sites include General Practices (GPs), Commonwealth Vaccine Clinics (CVCs), Community Pharmacies (CPs), and Aboriginal Controlled Community Health Services (ACCHS). As of 2 September August 2022, there are 9,728 sites across all jurisdictions which are actively participating in the vaccine rollout. The number of active sites change weekly, with over 10,000 active sites during peak periods of the rollout. Sites are not automatically withdrawn from the program during periods of low activity which ensures that sites can easily place a new or urgent order if demand increases unexpectedly (see Table 5).

	Channel						
Vaccine product	GP	CVC	Pharmacy	ACCHS	Total Primary Care only	State & Territory	Total Primary Care and State & Territory
AstraZeneca	5,099	111	3,236	149	8,595	65	8,660
Moderna 6 years+ (Red)	988	30	3,531	23	4,572	40	4,612
Novavax	1,643	41	1,721	19	3,424	44	3,468
Pfizer 12 years+ (Purple)	5,452	115	2,652	168	8,387	137	8,524
Pfizer 5-11 years (Orange)	4,513	101	1,975	137	6,726	109	6,835
Total	5,673	115	3,610	178	9,576	152	9,728

Table 5: Primary Care and state and territory vaccination sites by vaccine type.[65]

Vaccines procured by Australia were split via allocations between jurisdictions, general practice, pharmacies and other primary care channels to promote a variety of access points for individuals (see Figure 21). Vaccines were distributed on a per capita basis between jurisdictions, and dynamic re-allocation allowed supply to be shared between Primary Care and state health where unordering was observed. This ensured that per capita allocations could be maintained, and vaccines were accessible across Australia.

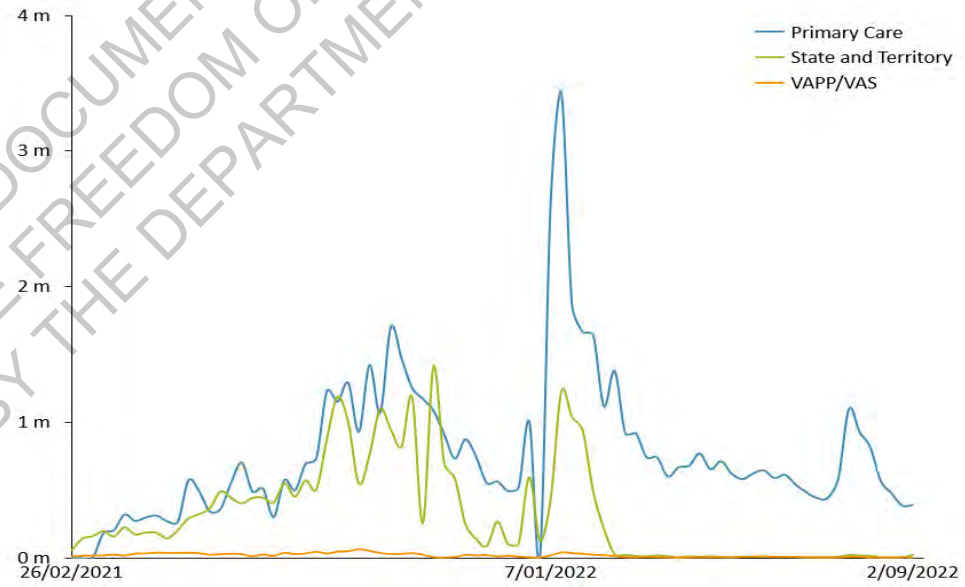

Figure 21: Weekly dose orders by site type.[66]

[65] Provided by Department of Health and Aged Care, data as at 1 September 2022.
[66] Provided by Department of Health and Aged Care, data as at 2 September 2022.

Primary Care sites have administered the majority of vaccine doses to date. State and territory hubs, also known as 'mass vaccination sites', were integral at the beginning of the program, as low supply limited the number of sites which could participate in the program and high throughput was required to increase the speed of the rollout and mitigate wastage from open multi-dose vials.

As Primary Care sites, particularly General Practice and pharmacy, built capacity and took on a larger share of both allocations and administrations, states and territories have been able to decrease contributions to vaccine administration (see Figure 22). As such, several state and territory hubs have now largely ceased operation. Despite the high efficiency of Primary Care sites in a business-as-usual operating environment, the ability to stand-up state and territory hubs rapidly would be required to meet future periods of high demand including in an emergency.

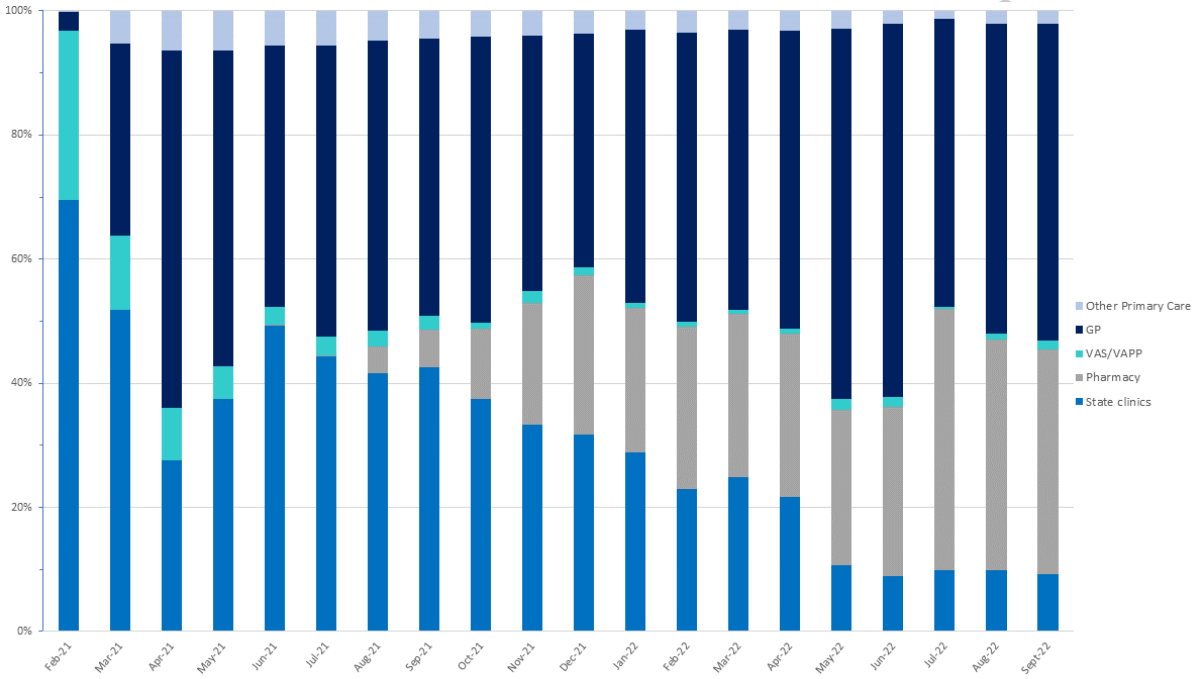

Figure 22: Proportion of doses administered by channel per month.[67]

The proportion of vaccines administered by state and territory hubs has decreased over time with general practice and pharmacy now administering most vaccines. The ability to quickly stand-up mass vaccination clinics should be retained in the event of an emergency or period of high demand.

In addition to static sites, vaccines were also made available to certain vulnerable or priority cohorts through 'in-reach' vaccination providers. This additional administration channel ensured that vaccines could be more easily accessed across Australia, and that individuals who could not easily travel to a static site were not inadvertently missed. Vaccine Administration Service (VAS) providers were contracted, first individually and later under the Vaccine Administration Providers Panel (VAPP), to provide vaccinations in pop-up clinics (see Table 6). Through this arrangement, VAPP providers provided up to five rounds of in-reach vaccination at Residential Aged Care Facilities (RACFs) and Residential Disability Sites (RDSs), as well as bolstering the vaccine workforce at ACCHS or other clinic types.

[67] Provided by Department of Health and Aged Care, data as at 2 September 2022.

State/Territory	Number of VAS Sites	Number of VAPP Sites
NSW	1039	88
VIC	715	60
QLD	623	163
WA	248	17
SA	238	51
TAS	72	15
ACT	31	0
NT	20	5
Total	2981	399

Table 6: Clinics run by VAS and VAPP by state and territory.[68]

The Royal Flying Doctors Service (RFDS) was also contracted to deliver and administer vaccines to rural and remote areas to run pop-up clinics. Both VAPP and RFDS vaccine providers worked alongside ACCHSs to provide vaccinations to Indigenous communities to increase access.

There has been criticism of the timeliness of rollout of the in reach programs which is beyond the scope of this review to examine.

6.5 Wastage

Vaccine wastage occurs when doses are not administered and must be disposed of. The World Health Organization (WHO) estimates that over 50% of all vaccines globally are wasted.[69] At the beginning of the global COVID-19 vaccine effort, WHO emphasised that in a supply constrained environment, 'every wasted dose represents a missed opportunity for vaccination'.[70] In the early stages of the vaccine rollout, Australia was successful at minimising wastage.

Vaccine supply, administration, and demand has been closely monitored for the duration of the program, with all sites required to report wastage to the Department (see Figure 23 and Figure 24). When vaccine supply was constrained and demand was high, vaccine wastage in Australia remained below 5% until the end of 2021 and below 10% until June 2022.

[68] Provided by Department of Health and Aged Care, data as at 1 September 2022.
[69] World Health Organisation, *Monitoring vaccine wastage at country level: guidelines for programme managers*, WHO, May 2005, accessed 17 August 2022.
[70] World Health Organisation, *Monitoring COVID-19 vaccination: considerations for the collection and use of vaccination data: interim guidance*, WHO, 3 March 2021, accessed 17 August 2022.

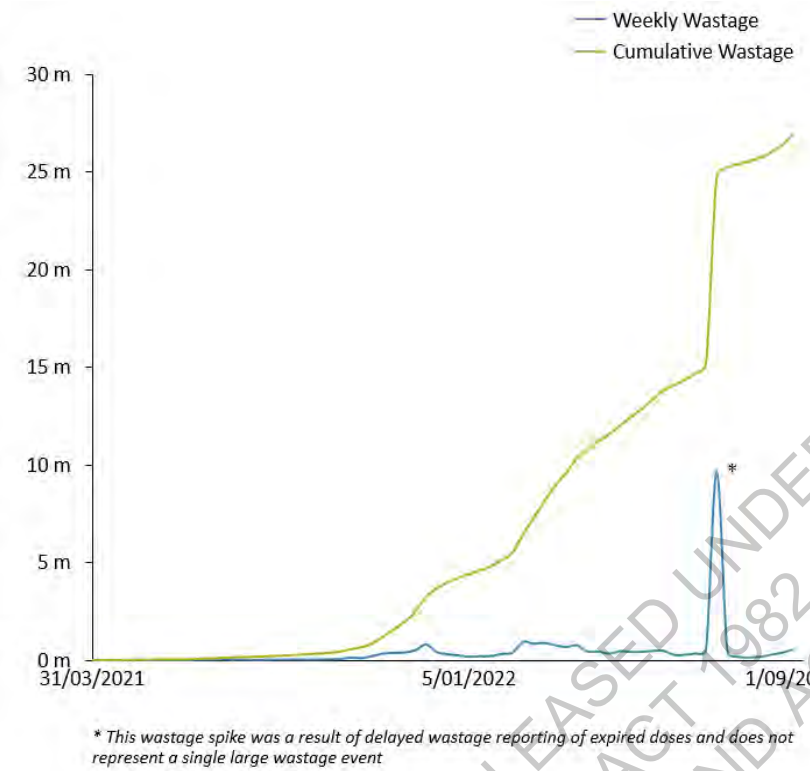

Figure 23: Wastage in Australia from the commencement of the program in March 2021 until the end of July 2022.[71]

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As demand reduced, wastage increased as the focus shifted from administering every vaccine, to ensuring that every opportunity to vaccinate was taken. Often this meant sites would only administer one or two doses from a multi-dose vial as once opened the shelf-life of the vaccine is greatly reduced. The current total vaccine wastage across all vaccine types supplied to Australia is 16.8%.[73]

[71] Provided by Department of Health and Aged Care, data as at 2 September 2022.
[72] Provided by Department of Health and Aged Care, data as at 2 September 2022.
[73] Provided by Department of Health and Aged Care, data as at 2 September 2022.

The WHO defines two types of wastage: wastage in closed vials and wastage in open vials. Wastage in closed vials can occur at all points of the vaccine program. The main causes of this wastage include errors in storage or handing, particularly Cold-Chain Breaches (CCBs) and expiry of doses when frozen (mRNA vaccines only) or thawed. CCBs often occur during transport when vials of vaccine product are exposed to temperatures outside the acceptable storage conditions due to the complexities of maintaining the temperatures required and the time-in-motion limitations.

This has been a particular challenge for the frozen Pfizer mRNA vaccine which must be kept at temperatures of –90°C to –60°C in transport. Thawed vaccines also have strict Cold-Chain requirements. Vaccines can expire both when frozen and when thawed. Vaccines arrive from the manufacturers frozen, as this state provides the longest shelf life for each product and the shelf life when thawed is reduced and dependant on the date of thawing (see Table 7).

Vaccine	Frozen Shelf Life	Thawed Shelf Life	Open-Vial Shelf Life
Moderna	9 months at -50°C to -15°C	30 days at 2°C to 8°C Within the 30 days, 12 hours can be used for transportation	19 hours at 2°C to 25°C after initial puncture
Novavax	N/A	9 months at 2°C to 8°C	6 hours at 2°C to 25°C after initial puncture
Pfizer > 12 years Purple cap	15 months at –90°C to –60°C OR 2 weeks at -25°C to -15°C	1 month at 2°C to 8°C	6 hours at 8°C to 25°C after dilution
Pfizer 5 – 11 years Orange cap	12 months at -90°C to -60°C	10 weeks at 2°C to 8°C	12 hours at 8°C to 25°C after dilution
Astra Zeneca	N/A	6 months at 2°C to 8°C	6 hours after initial puncture (up to 30°C) OR 48 hours after initial puncture (2°C to 8°C)

Table 7: Shelf-life of current vaccine products.[74]

Wastage also occurs in open vials of vaccines at administrations sites. This wastage is harder to eliminate than wastage in closed vials because of the significantly reduced shelf-life of vaccine products after opening. This wastage occurs for multiple reasons, including being unable to use all the doses in Multi-Dose Vials (MDVs) within the open-vial shelf-life, errors in drawing up or diluting the vaccines for administration. All vaccine products currently available in Australia are manufactured in MDVs: Pfizer 12+ vials contain 6 doses and Pfizer 5-11, Novavax, and Astra Zeneca vials contain 10 doses. Moderna MDVs contain 10 primary course doses or 20 booster doses.

Over the course of the vaccine program, a wide array of controls were implemented to reduce wastage of all types. The logistics context within Australia, a large country requiring long transit times for vaccines, including to very rural and remote locations, has presented various challenges to Cold-Chain processes. To reduce closed vial wastage, controls have been built into these processes including temperature monitoring, custom product packaging to suit the external temperatures in each region, regular meetings with logistics partners to quickly identify and resolve issues and providing freezers to ACCHS in rural and remote areas, RFDS and jurisdictions for the storage of frozen mRNA vaccines.

A consumables provider panel was established to ensure supply of the consumables to draw up and dilute vaccines (e.g. low dead-space syringes) to ensure all doses in each vial can be utilised. Where doses were not ordered by sites for domestic use, significant effort has been made by the program, in collaboration with DFAT, to donate closed vials to international partners. As at 2 September 2022, Australia has donated over 23.6 million doses of vaccine product from Australia's supplies and 17.2

[74] Provided by Department of Health and Aged Care, data as at 13 September 2022.

million doses through UNICEF.[75] Ongoing effort to donate doses continues, however global vaccine supply has surpassed demand and is now limiting the efficacy of donation as a control for wastage.

Due to the shifting nature of the supply and demand landscape for vaccines, wastage thresholds and expectations have been revised. The WHO acknowledges that vaccine programs should expect increases in wastage as the proportion of the population which is vaccinated increases.

s47E, s47G, s34(3)

> *Whatever measures are taken to reduce vaccine wastage, they should not compromise immunization coverage. If a selected approach to reducing vaccine wastage results in reducing immunisation coverage, other approaches should be considered.*[76]

The Purchase Administration (PA) ratio refers to the number of doses required to be purchased to meet forecasted vaccine administrations. Procured doses must be greater than forecast administrations to ensure access across Australia by maintaining the number of participating sites as well as accounting for wastage at sites and minimum ordering values.

The PA ratio is affected by supply chain requirements and uptake of vaccines. Eligibility and different distribution models: on-demand or fixed schedule, materially impacts the PA ratio. A higher PA ratio will result in more wastage. The PA ratio of COVID-19 vaccines has increased as the rollout has progressed (see Figure 25).

s47C, s34(3)

[75] Provided by Department of Health and Aged Care, data as at 2 September 2022.
[76] World Health Organisation, *Monitoring vaccine wastage at country level: guidelines for programme managers*, WHO, May 2005, 17 August 2022.
[77] Provided by Department of Health and Aged Care, data as at 2 September 2022.

s47C, s34(3)

Ongoing wastage policy should:

- Acknowledge wastage will increase when supply is high and demand is low. Levers to increase demand such as adopting more permissive eligibility settings which align with the TGA indications for approval and clear public health messaging are critical to reducing wastage;
- Ensure efforts to reduce wastage do not impede the ability to provide sufficient vaccines to ensure all Australians can get vaccinated if required;
- Continue controls which exist to mitigate most wastage that occurs during transport and at vaccination sites; and
- Preference the levers which reduce wastage earliest in the vaccine life cycle, including flexible supply schedules, extending shelf-life, and donation.

Wastage is expected in an oversupply environment. Eligibility and priority use recommendations can affect wastage.

6.6 New and emerging vaccines

Australia's COVID-19 vaccine strategy has shifted multiple times in response to changes in the vaccines landscape; most notably the shift to mRNA vaccination following the increased risks of serious thrombotic vaccine side-effects associated with the AstraZeneca viral vector vaccine.[78] These shifts have been informed by available research from independent sources (e.g., the WHO) as well as reports from international vaccine programs (e.g., UK, Israel, USA).

Studies note increased immune evasion by new COVID-19 variants due to increased difference from the ancestral strain may reduce the efficacy of existing vaccines going forward.[79] As such, vaccine manufacturers have commenced development of vaccines which specifically target the original Omicron variant to induce a stronger and broader immune response with similar safety profiles to the original vaccines.[80]

According to the WHO, there are a total of 359 vaccine candidates in development in both clinical and pre-clinical stages (see Figure 26).[81] Only a small number are at Phase 4 where candidates seek licensing and registration.

[78] ATAGI, 'Joint statement from ATAGI and THANZ on Thrombosis with Thrombocytopenia Syndrome (TTS) and the use of COVID-19 Vaccine AstraZeneca', *Department of Health and Aged Care,* 23 May 2021, accessed 09 August 2022.
[79] J Bowen et al., 'Omicron spike function and neutralizing activity elicited by a comprehensive panel of vaccines', *Science,* 2022, July 2022.
[80] S Chalkias et al., 'A Bivalent Omicron-containing Booster Vaccine Against Covid-19', *medRxiv,* 2022, 25 June 2022.
[81] World Health Organisation, *COVID-19 vaccine tracker and landscape,* WHO, 09 August 2022, accessed 12 August 2022.

Figure 26: COVID-19 vaccines in the clinical phase of the development pipeline.[82]

New vaccination strategies are being explored by developers due to concerns over potential reduced efficacy of existing vaccine products against Omicron and future variants. Some of the techniques being considered include variant specific vaccines, vaccines that target multiple variants, targeting different sites on the SARS-CoV-2 virus, or broadly protective vaccines that provide increased protection against multiple variants.[83]

Mucosal vaccines for nasal or oral administration are also in development and may provide greater immunity against mucosal infections, and so better decrease spread, in contrast to current vaccines which are less effective against infections but more effective against severe illness.[84]

Work to streamline the development of variant specific vaccines will be critical to ensure vaccines can be made available in a timely manner as variants emerge to have the greatest impact. Broadly protective vaccines are a theoretical approach to designing vaccines which target the features of SARS-CoV-2 (or indeed all coronaviruses) that may provide immunity against all existing and future variants.[85] Broadly protective vaccines are still in pre-clinical stages of development and have not yet commenced human trials.

As it is currently not known which strategies will be most effective due to the uncertain nature of the COVID-19 pandemic, ongoing effort to support research and development should aim to improve available tools to prevent infections, hospitalisations and, deaths until 'COVID-stable' is achieved. A focus on the science of new vaccine products and potential approaches to population health will be critical for ongoing engagement with vaccine manufacturers to identify products that will provide the greatest protection during the ongoing uncertainty of the pandemic.

New variant specific, bivalent and broadly protective vaccines are being researched and developed.

s47C, s47G, s34(3)

On 29 August, the TGA provisionally approved Moderna's BA.1 Omicron bivalent COVID-19 vaccine, for use as a booster dose in adults 18 years and over.[86] s47C, s47G, s34(3)

The Moderna bivalent vaccine has also been approved for use in the UK.[87] Pfizer's BA.1 bivalent candidate has been granted a provisional

[82] WHO, 'COVID-19 vaccine tracker and landscape', *WHO*, 09 August 2022, accessed 12 August 2022.
[83] D Altman, R Boyton, 'COVID-19 vaccination: The road ahead', *Science,* 2022, Vol. 375, pp. 1127-1132.
[84] V Mouro, A Fischer, 'Dealing with a mucosal viral pandemic: lessons from COVID-19 vaccines', *Mucosal Immunology*, 2022, Vol. 15, pp. 584–594.
[85] L Geddes, 'Could a variant-proof coronavirus vaccine be within reach?', *GAVI*, 08 July 2022, accessed 15 August 2022.
[86] Therapeutic Goods Administration, *TGA provisionally approves Moderna bivalent COVID-19 vaccine for use as a booster dose in adults* [media release], TGA, 30 August 2022, accessed 5 September 2022.
[87] Medicines & Healthcare products Regulatory Agency, *First bivalent COVID-19 booster vaccine approved by UK medicines regulator* [media release], MHRA, 15 August 2022, accessed 9 September 2022.

determination by the TGA and is currently under evaluation.[88] s47C, s34(3) [redacted]

Both Moderna and Pfizer have also commenced manufacturing Omicron BA.4/5 bivalent vaccines. On 31 August 2022, the FDA provided emergency use authorisation for Pfizer's bivalent for people over 12 years of age, and Moderna's bivalent for people over 18 years of age.[89] s47C, s34(3) [redacted]

s47C, s42, s34(3) [redacted]

s47C, s34(3) [redacted]

Initial trial data, based mainly on antibody responses, show that variant specific vaccines may be more effective than the original wildtype vaccines against Omicron variants.

7 Access to COVID-19 Treatments

At the onset of the pandemic in early 2020, there were no therapeutic options available to treat COVID-19. Widespread trials of many potential treatments led to early evidence suggesting that Veklury (remdesivir) was effective against SARS-CoV-2. Many products have been suggested as possible treatments and ongoing research and evaluation and is needed to ensure that the products prescribed to patients are safe and effective.

7.1 Procurement

Australia has continued to evaluate emerging evidence to enable procurement of effective treatments. In mid-2020, the TGA provisionally approved Veklury as the first treatment of COVID-19 in Australia.[91] This was followed by initial limited advance purchases of Veklury to be held in the National Medical Stockpile for distribution to state hospitals.

The availability of treatments alongside vaccines has become an important component of the health response to COVID-19.

Treatment procurement decisions were made in an extremely competitive, supply constrained environment, like that of vaccines. Decisions on procurement were made prior to treatments

[88] Therapeutic Goods Administration, *TGA grants provisional determinations to Pfizer for COVID-19 vaccines to target Omicron variant* [media release], TGA, 6 July 2022, accessed 6 September 2022.
[89] US Food and Drug Administration, *FDA Authorizes Moderna, Pfizer-BioNTech Bivalent COVID-19 Vaccines for Use as a Booster Dose* [media release], FDA, 31 August 2022, accessed 9 September 2022.
[90] This attachment is protected under legal privilege.
[91] Therapeutic Goods Administration, *COVID-19 treatment: Gilead Sciences Pty Ltd, remdesivir (VEKLURY)* [media release], TGA, 17 August 2022, accessed 22 August 2022.

receiving regulatory approval, and in many cases while the treatments were still undergoing clinical trials (see Figure 27).

s47E, s47G, s34(3)

Investments were made at risk. Failed clinical trials, denial of regulatory approvals, length of time to market, and changes in dominant variants and efficacy of treatments which would render treatments ineffective were all risks. These procurement decisions were informed by the SITAG prior to consideration by Cabinet and the Department entering into APAs.

The procurement of treatments in late 2021 aligned with National Cabinet decisions to transition away from suppression of community transmission to focusing on prevention of serious illness, hospitalisation, and death. This is supported by high levels of community protection of vaccination which provide strong protection against serious illness but less protection against infection. Treatments were available to provide further protection to people at increased risk of developing severe disease as a result of increased COVID-19 cases.[93]

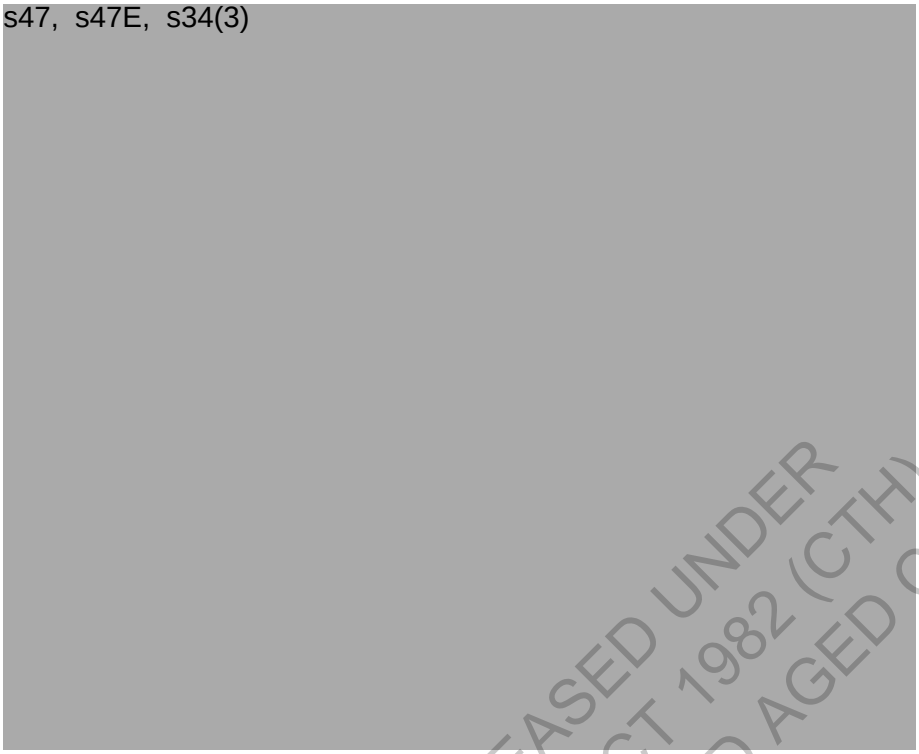
The level of supply required for the Australian population will vary in response to changing dominant variants, spikes in cases, and changing effectiveness of treatments. Advanced planning is required, using best evidence available, to manage outbreaks and emerging variants in a future supply environment, while also optimising secured supplies to minimise wastage.

Australia has entered into APAs with several manufacturers/sponsors, including Gilead Sciences, GlaxoSmithKline (GSK), Roche, Merck Sharp and Dohme (MSD), Pfizer, and AstraZeneca to secure supply of treatments. These agreements set out the terms and conditions for supply of treatments. Most agreements were executed in late 2021 to guarantee supply of treatments in late 2021 and across 2022.

Through these APAs, Australia procured a diverse range of treatments options which target different stages of COVID-19 (see Figure 28).

[92] Provided by Department of Health and Aged Care, 3 August 2022.

[93] Australian Government, 'National Plan to Transition Australia's National COVID Response', *Department of the Prime Minister and Cabinet*, 02 July 2021, accessed 18 August 2022.



Variations have been made to a number of these APAs to allow for greater supply, or to amend supply schedules and conditions to allow Government to respond to new dominant variants of COVID-19 and changes in global supply and demand.

This has included variations to the agreements with Pfizer and MSD to enable supply of antiviral treatments though the PBS.

In addition to the treatments procured through APAs, other treatments for COVID-19 are available. These are mostly procured directly by state and territory Governments for utilisation in public hospitals. This includes treatments previously approved for use for other indications in Australia, now being used to treat people with COVID19, including tocilizumab (Actemra), dexamethasone, baricitinib (Olumiant) and sarilumab (Kevzara).

7.1.1 Rapid Health Technology Assessment Process for COVID-19 Treatments

To enable rapid assessment of new COVID-19 therapeutics, a streamlined rapid Health Technology Assessment (rHTA) process was introduced from 2021. This new process has been used to assess promising new COVID-19 treatments and inform an assessment of comparative effectiveness, safety, and cost-effectiveness.

The rHTA process is largely undertaken in parallel to the TGA registration process, utilising information submitted to the TGA and the Department such as the TGA dossier and commercial proposals from the sponsor for procurement. This allows assessment of cost-effectiveness by the Department outside of the usual PBAC submission evaluation process in a shorter timeframe (relative to the usual PBAC submission evaluation cycle time).

rHTAs have been utilised by the SITAG as an input to advice to the Department and Government to secure the most effective and suitable COVID-19 treatments through APAs. They have also been used to streamline PBAC consideration of COVID-19 treatments.

[94] Provided by Department of Health and Aged Care, data as at 2 September 2022.

7.2 COVID-19 Treatments Efficacy

The emergence of Omicron subvariants of COVID-19 has significantly impacted the efficacy of monoclonal antibody treatments. These variants have mutations on the spike protein which has reduced the ability of monoclonal antibodies to recognise and bind to SARS-CoV-2.

Omicron variants have had a significant impact on the effectiveness of Xevudy (sotrovimab) and Ronapreve (casirivimab and imdevimab) and are no longer recommended for use against the current dominant variants. There is significant risk that emerging variants will continue to impact effectiveness of monoclonal antibody treatments.

Despite the wide impact of Omicron strains on monoclonal antibody treatments, the prevention of viral replication by antivirals is less likely to be hindered by emerging SARS-CoV-2 variants of concern, compared to monoclonal antibody therapies, as antivirals possess a higher genetic barrier to the development of resistance. Antiviral treatments are also more robust and scalable compared to monoclonal antibody treatments.

Through *in vitro* studies, Veklury (remdesivir), Paxlovid (nirmatrelvir and ritonavir), Lagevrio (molnupiravir) and Evusheld (tixagevimab and cilgavimab) have all demonstrated retained neutralising activity against all omicron strains including BA.4 and BA.5 variants.[95]

An overview of the clinical efficacy against variants of concern, real-world effectiveness, safety, and key clinical trials is outlined in Attachment 5.

Australia has procured a range of treatments which are available through state hospitals and community pharmacy. It is important to continue to monitor the ongoing efficacy of COVID-19 treatments against the current dominant strains and latest clinical research.

7.3 Distribution and Access

Approved treatments have been dispensed via a number of channels over the course of the pandemic. Patients have accessed these treatments through hospitals (as both inpatients and outpatients), via state community health infrastructure, through Residential Aged Care Facilities, Aboriginal Community Controlled Health Organisations, the Rural Flying Doctors Service, pharmacy and general practice. The distribution channels used to deliver these treatments varies in part with the funding mechanism used to procure them (e.g. PBS medicines are dispensed by pharmacies) and the method of administration (e.g. IV products cannot be used at home).

Different procurement and distribution channels can make it difficult for sponsors to manage supplies of stock (because it is hard to get a whole of system view) and for patients to know where and how to access treatments. Confusion about eligibility and recommendations for use compounds this problem.

Since the first procurement of COVID-19 treatment in mid-2020, COVID-19 treatments have been procured, held, and distributed by the NMS directly to state and territories. See Attachment 18.

[95] E Takashita et al., 'Efficacy of Antibodies and Antiviral Drugs against Omicron BA.2.12.1, BA.4, and BA.5 Subvariants', *New England Journal of Medicine*, 2022. 387(5): p. 468-470.

Once provided to the states, each state and territory is responsible for the distribution of treatments within their jurisdiction as per their COVID-19 care arrangements. In-hospital treatments, such as Veklury, are accessed through state hospital settings for patients admitted due to hospitalised due to the severity of their COVID-19 symptoms.

Intravenous (IV) treatments, such as Xevudy, Ronapreve, and Veklury, for the treatment of mild-moderate COVID-19 are delivered by states and territories through out-patient clinics following prescription from a qualified medical professional. Patients are identified through COVID-19 care arrangements following positive COVID-19 polymerase chain reaction (PCR) test or registering a positive rapid antigen test (RAT).

Supplies of the antivirals are available through out-patient clinics and hospital pharmacies to patients identified through COVID-19 care arrangements, targeting vulnerable groups following positive COVID-19 PCR test or registering a positive RAT test.

From early 2022, with the TGA provisional approval and supply of oral antiviral treatments, further distribution networks were required to increase access points particularly for the most vulnerable groups.

From February 2022, oral treatments were pre-deployed from the NMS to ACCHS and the RFDS. Stocks of Lagevrio have been provided to all RACFs to ensure oral antivirals were available for administration to eligible patients once prescribed.

Supplies of Lagevrio and Paxlovid continue to be supplied from the NMS to state and territory governments, RACFs, ACCHSs and the RFDS to help manage COVID-19 outbreaks, and to provide access to the antivirals where supply cannot be accessed through the PBS.

Supplies of Actemra (*tocilizumab*) for the treatment of COVID-19 are procured by states and territories for supply to patients in public hospitals. Prior to the pandemic, Actemra was commonly used to treat rheumatoid arthritis and other arthritic conditions with supplies accessed through the PBS and procured by states and territory governments for supply to patients in some state hospitals.

In July 2021, the WHO recommended *tocilizumab* for the treatment of patients with severe COVID-19. This recommendation was also made by the CET. As a result, there has been broad off-label use in public hospitals for the treatment of COVID-19 in adults requiring supplemental oxygen.

This recommendation resulted in a demand spike and subsequent critical global supply shortage. On 1 December 2021, the TGA granted provisional approval to Roche Products Pty Ltd for the use of Actemra for the intravenous treatment of COVID-19 in hospitalised adults aged 18 years and older who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation.

The TGA, working in collaboration with a wide range of stakeholders including the Medicine Availability Working Group (comprising representatives from state and territory health departments, the sponsor, pharmaceutical wholesaler), the Australian Rheumatology Association, and the CET, developed guidelines and advice to conserve stocks nationally for patients who have no alternative therapies.[96]

As global supply shortages have resolved in mid-2022, all supply conservation measures have been lifted.

The supply of Actemra has shown that an exponential spike in demand requires mechanisms to ensure patients without alternative treatments or at the highest risk receive priority access to treatment.

[96] Therapeutic Goods Administration, *Joint statement: Supply allocations of intravenous tocilizumab (Actemra) during serious shortage* [media release], TGA, 07 October 2021, accessed 22 August 2022.

Evusheld is the most recent therapeutic to be supplied to state and territories. As Evusheld is a pre-exposure prophylaxis rather than a treatment for COVID, each state and territory has developed specialised distribution points of Evusheld outside of the normal COVID care pathways. Evusheld is being prioritised for pre-exposure prophylaxis in severely immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or due to underlying medical conditions or treatments that compromise the body's immune system and likely to derive the most benefit. State and territories are targeting supply of Evusheld through in-patient and out-patient settings in their respective jurisdictions.

High levels of utilisation have been reported and there is a risk of supply shortage if high use continues or if there is any change in use criteria. This needs to be monitored in real time.

s47E, s47G, s34(3)

PBS listing requires a positive recommendation from the PBAC and agreement between the sponsor and the Government on any measures the PBAC has advised as necessary to ensure effectiveness and cost-effectiveness. s47E, s47G, s34(3)

s47E, s47G, s34(3)

Despite procuring a substantial number of the oral treatments for Australians, utilisation has been relatively slow. The NMS and state and territory infrastructure has proven of limited effectiveness for distribution of community-based medicines (see Table 9). This role is outside of the design and scope of the current NMS model.

Access Points	Hospital Treatment	State Out-Patient Clinics	ACCHS	RACFs	RFDS	Community Pharmacy
Paxlovid	No	✓	✓	*	✓	✓
Lagevrio	No	✓	✓	✓	✓	✓
Veklury	✓	✓				
Xevudy	No	✓			✓	
Ronapreve	No	✓				
Evusheld	No	✓				
Actemra	✓					

** Paxlovid is also available to patients in RACFs through PBS prescriptions supplied through pharmacies.*

Table 9: Access points for treatments by treatment type.[97]

s47C, s47E, s34(3)

[97] Provided by Department of Health and Aged Care, data as at 2 September 2022.

***Recommendation 6**: New mechanisms to manage stock held by the NMS for use in an ongoing pandemic or epidemic should be developed as a matter of urgency to enable greater transparency about and access to stocks held.*

On 1 March 2022 and 1 May 2022, Lagevrio and Paxlovid were listed on the PBS as treatments for people with COVID-19 who are at risk of developing severe disease.

The supply of Lagevrio through the PBS has been managed by MSD as the Sponsor, s47E, s47G, s34(3)

The PBS listing for medicines enables eligible patients to access this medicine from their local community pharmacy on a prescription from their doctor or authorised nurse practitioner. s45, s47, s47E, s34(3) Listing of the oral antivirals on the PBS has allowed for supplies of the medicines to be accessible at the over 5,700 pharmacies across Australia.

Both medicines are listed on the PBS as 'General Schedule' and are dispensed under section 85 of the *National Health Act 1953*. This has enabled community pharmacies to supply of both medicines under the CSO. Under the requirements of the CSO Funding Pool, which funds wholesalers to distribute PBS medicines, wholesalers must supply both Lagevrio and Paxlovid to community pharmacies within 24 hours of order cut-off times, including to rural and remote pharmacies. Due to the cost of the medicines, there has been some hesitancy for pharmacies to hold large stocks of the oral antivirals on shelves, instead relying on CSO wholesalers to supply within 24 hours.

The recent Omicron BA.4/BA.5 wave led to spikes in demand due to increased case numbers and expanded PBS eligibility criteria. Some supply shortages were reported and alternative supply points, such as state and territory governments, RACFs and ACCHSs, were important in ensuring people accessed needed medicines within 5 days of symptom onset if they could not readily access supply through pharmacy.

A systems approach to distribution and clear communication to patients about eligibility and access is needed to ensure available treatments are utilised to mitigate the impact of COVID-19.

s47C, s34(3)

It remains important for Government and product sponsors to monitor supply of antivirals to ensure adequate supplies of each medicine are available across Australia, especially in high demand scenarios. See Section 8.2.

PBS listing alone does not guarantee that needed stock will be available in the event of a demand spike.

Recommendation 7: *The Department of Health and Aged Care should work with sponsors to ensure that adequate supplies of therapeutics are available to meet reasonably anticipated demand for the next two years. Mechanisms such as guarantees for minimum supply should be explored to ensure availability and access.*

s47E, s47G, s34(3)

s47C, s34(3)

7.4 Eligibility

Eligibility criteria and prescriber confidence are key to ensuring access to treatments and therapeutics. These vary with the distribution mechanism (State, PBS, and Community based organisations).

Eligibility depends on efficacy, with priority given to those most at risk of severe disease and death particularly in a supply constrained environment. Relative cost effectiveness is also relevant.

Criteria have been narrowly targeted during the last 12 months but have been relaxed more recently.

Studies are currently underway to assess the wider use of treatments, particularly in some occupation groups.

[98] Provided by Department of Health and Aged Care, data as at 4 September 2022.

With considerable disruption to work and education still being experienced, the potential benefit of wider eligibility and use of efficacious treatments (particularly where there are sunk costs) should be considered.

7.4.1 State and Territory Access Criteria

Eligibility for and access to COVID-19 treatments distributed by state and territory governments is decided by each jurisdiction based on their COVID-19 care arrangements. Criteria in each jurisdiction may take into account factors such as the PBS eligibility criteria, recommendations from the CET, and the TGA provisional registration indications. Access criteria are utilised by states to target and identify patients following positive COVID-19 PCR test or registering a positive RAT test. Further details on the TGA indications, CET Recommendations, and PBS eligibility criteria for each treatment are at Attachment 18.

7.4.2 Access Criteria in community-based organisations (RACFS, ACCHSs and RFDS)

The PBS eligibility criteria may also be taken into account by health professionals in the prescribing of the oral antiviral medicines supplied through ACCHS, RACFs and RFDS. However, unlike prescriptions for subsidised medicines, there is no requirement for prescribers to follow the PBS criteria for non-PBS prescriptions.

7.4.3 PBS Eligibility

Eligibility criteria on initial listing were restrictive. As a consequence, utilisation of treatments available on the PBS was very low.

These eligibility criteria were expanded on 11 July 2022. Currently PBS-subsided prescriptions of Lagevrio and Paxlovid are limited to patients with COVID-19 who are:

- aged 70 years or older irrespective of whether they are symptomatic;
- aged 50 years or older with two or more risk factors for severe disease;
- aged 30 years, who identify as Aboriginal or Torres Strait Islander with and two or more risk factors for severe disease; or
- aged 18 years or older who at risk of progressing to severe disease due to their immunocompromised status.

Initial criteria were designed to target populations who most benefit from treatments based on available clinical advice, availability of supply, and estimated usage. As supply increased, the PBAC recommended expanded eligibility to support greater access to additional patients likely to benefit. This recommendation was informed by recent evidence on efficacy and safety of these medicines, utilisation patterns, changing epidemiology of COVID-19, and advice from clinical groups.

7.5 Utilisation and wastage

Utilisation is affected by both eligibility criteria and actual access to products. Prescriber knowledge of both the product and confidence in its use are material to utilisation. Patients must also know how and when to seek treatments. Demand can also influence prescribing behaviour.

To date, utilisation has been materially lower than expected, s47C, s34(3)

s47, s47E, s34(3)

With the combination of the expansion of the PBS criteria on 11 July 2022 and the increase in COVID-19 cases associated with the Omicron BA.4/BA.5 wave in Australia, uptake of the oral treatments through the PBS increased, peaking in the week of 18 July 2022. Prescription levels of the antivirals has steadily decreased since following the downward trend of COVID-19 case numbers in Australia (see Figure 30).

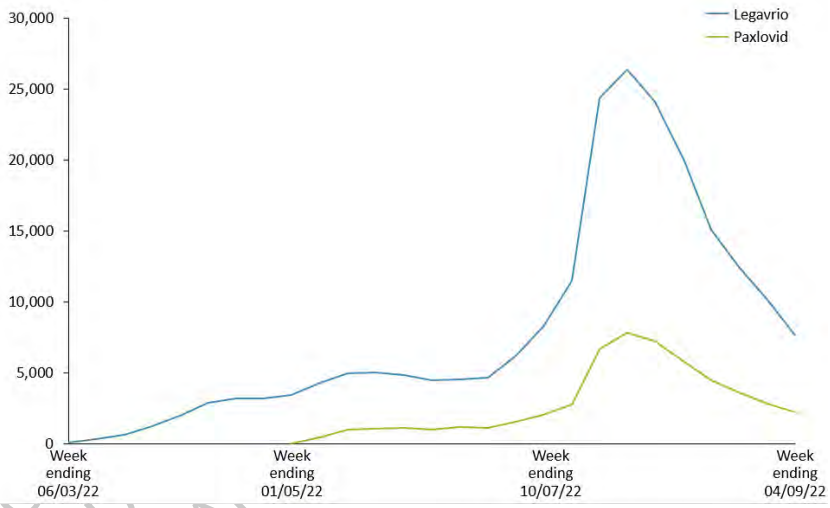


Figure 30: Utilisation of COVID-19 oral antiviral treatments through the PBS.[100]

s47C, s34(3)

To date utilisation, particularly through the NMS channels, has been lower than expected. While states have shown eagerness to distribute hospital-based treatments, the distribution of community-based medicines has proved more difficult.

s47C, s47E, s34(3)

[99] Provided by Department of Health and Aged Care, data as at 4 September 2022.
[100] Provided by Department of Health and Aged Care, data as at 4 September 2022.

s47C, s34(3)

s47C, s47E, s34(3)

States and territories have been encouraged to use the NMS stocks to supplement PBS use to enable greater access to oral antivirals. s47C, s34(3)

As discussed in Section 6.2, the Omicron variants have had a significant impact on the efficacy of Xevudy (*sotrovimab*) and Ronapreve (*casirivimab* and *imdevimab*). s47C, s34(3)

s47C, s34(3)

Some wastage of therapeutics is to be expected as stock begins to expire due to slower than anticipated utilisation and treatments losing efficacy against current variants.

7.6 New and emerging treatments

Although there are several treatment options available, each new strain of SARS-CoV-2 looms as a threat which could render existing therapies ineffective. This underscores the importance of continued investments in research and development to ensure sustained innovation into new treatment options to ensure health systems are prepared to respond rapidly to future pandemics. In addition, to overcome the potential threat of acquired drug resistance, the development of antivirals aimed at different targets, or single multimodal treatments to attack the virus on multiple fronts is needed.[103]

Antibodies against specific sites on the SARS-CoV-2 virus and with extended half-life should also be investigated to limit the need for repeated use in pre-exposure prophylaxis.[104] Research is underway into new treatments globally and there are emerging COVID-19 treatments some of which have promise. See Attachment 20.

[102] Provided by Department of Health and Aged Care, data as at 4 September 2022.

[103] D Narayanan, T Parimon, 'Current Therapeutics for COVID-19, What We Know about the Molecular Mechanism and Efficacy of Treatments for This Novel Virus', *International Journal of Molecular Sciences*, 2022, 23(14): p. 7702.

[104] D Focosi et al., 'Monoclonal antibody therapies against SARS-CoV-2', *The Lancet Infectious Diseases*, 2022.

Ongoing monitoring of COVID-19 mutations and variants, including impacts on treatment efficacy, will be required.

8 Transitional arrangements

It is difficult to confidently predict the trajectory of the pandemic over the next two years. While the current outlook appears promising, it is not certain due to the potential for the emergence of new variants of concern and/or ongoing waves of infection. How long it will take before it is possible to transition to a 'COVID-stable' operating model is unknown and may be able to be better judged following the coming northern hemisphere winter. This makes current procurement decisions difficult.

The global market for new vaccines/therapeutics which effectively target new variants will continue to operate as a sellers' market. Purchasing decisions will need to be made in the context of excess demand. Manufacturers are also unlikely to produce products 'at risk'. Both factors are relevant to purchasing decisions.

Choices about what vaccines and treatments to procure depend on both availability (supply chain constraints) and risk appetite. The strong likelihood of shortage and stock-outs in the event of significant new variants or major waves of virus remains.

s47C, s34(3)

Policies, procurement, and delivery over the next two years should:

- *Encourage ongoing high levels of vaccination across the community for those that will benefit;*
- *Enable the Health Minister to operate in the transition period (before 'COVID-stable' is achieved) to manage the downside risk associated with the emergence of a serious new variant;*
- *Ensure that there is adequate and speedy access to vaccines and treatments by patients, if and when they are required;*
- *Provide maximum possible protection through vaccinations and treatments over the short to medium term to protect the vulnerable, limit hospitalisation and death, and allow the economy and health system to recover;*
- *Adopt a portfolio and redundancy approach to the procurement of vaccines and treatments, with acceptance of associated higher levels of wastage;*
- *Encourage a partnership approach with industry and sponsors ensuring transparency and optimal outcomes for Australian patients;*
- *Utilise existing and established distribution channels (primary care including general practice and pharmacies, and states and territories) and maintain capacity to ensure distribution of vaccines can be scaled up rapidly in the event of a need for high levels of vaccination for a new more virulent variant; and*
- *Facilitate decision-making which considers the ongoing public health management of the pandemic rather than the point in time relative risk (e.g. absolute risk of side effects as determined by TGA/medical analysis). Unless there are significant clinical differences, approaches should be simplified as much as possible to streamline and encourage public uptake.*

8.1 Vaccines

The principles articulated above are proposed as the basis for managing polices, procurement, and delivery of vaccines and treatments over the forthcoming period. In this context, future demand will be influenced by changes to the virus and resultant impact on infection and hospitalisation rates. Considering the wide range of potential pandemic changes and impacts, demand for COVID-19 vaccinations over the next few years may vary significantly depending on the number and severity of waves of COVID-19.

s47C, s34(3)

Forecasting required numbers of vaccines is an inexact science. Clear policy positions, risk frameworks, and understanding of the development pipeline, production issues, demand and delivery arrangements is needed to inform judgement and guide decision-making.

s47C, s47E, s47G, s34(3)

[105] Provided by Department of Health and Aged Care, data as at 2 September 2022.

s47C, s47E, s47G, s34(3)

On-demand ordering would significantly reduce the wastage of vaccine products in low and medium demand scenarios, and therefore reduce the total amount of vaccines required to meet demand in 2023 and 2024.

s47C, s34(3)

s47E, s47G, s34(3)

[106] Provided by Department of Health and Aged Care, data as at 2 September 2022.
[107] Provided by Department of Health and Aged Care, data as at 2 September 2022.

s47C, s34(3)

Australia's use of COVID-19 vaccines is currently heavily weighted towards mRNA vaccines. This is largely due to:

- the early use and high uptake of Pfizer in the rollout;
- later Novavax onboarding (once over 95% of adults in Australia were fully vaccinated); and
- recommendations by the ATAGI which currently limit the use of AstraZeneca and Novavax, including to older age groups or where or where mRNA vaccines are considered unsuitable as a booster dose respectively (see Attachment 16).

Paediatric COVID-19 vaccines for children under 12 years of age are solely met through mRNA vaccines as these are the only formulations approved for use in Australia. These are supplied by the manufacturers through well-established swap mechanisms in the APAs.

s47C, s34(3)

Two strategies are available to decrease the wastage of Novavax and reduce the number of additional mRNA vaccines required to meet predicted administrations:

- implementing less restrictive eligibility criteria; and
- working with the manufacturer to defer Novavax doses into 2024 where possible.

Australia will likely have an over-supply of Novavax in 2023. Australia could implement more permissive eligibility settings for Novavax to increase uptake and reduce the need for additional mRNA vaccines; and/or work with the manufacturer to defer delivery of doses into 2024.

Some additional mRNA vaccines are required in 2023 and s47C, s34(3)

The Moderna formulation for 6 month – 5-year-olds is also currently the only formulation approved for this age group.[108] It is critical sufficient supplies of this vaccine are maintained for vulnerable children.

Additional procurement of Moderna vaccines should be undertaken for 2023 to meet any anticipated shortfall in the number of mRNA vaccines required and to ensure access to vaccines for children under five years.

s47E, s47G, s34(3)

It is important to put these numbers into a broader context. Influenza is an endemic seasonal respiratory virus. Effective vaccines are available and there is widespread up take of these vaccines which help to prevent illness, severe disease, and death s47C, s34(3) In 2022, the TGA cleared 17.7 million doses of influenza vaccines which supported 11.0 million vaccinations to date (see Figure 33). Of these, just under half were procured privately. The combined voluntary (private) and recommended (subsidised/government funded) uptake provides a baseline for the minimum demand for COVID-19 vaccines in the future. [109] It also illustrates that wastage is expected even in well-established vaccination programs. Influenza vaccines have a 12-month shelf life so the true number of administrations and wastage will not be known until January 2023. However, previous administration data shows that most vaccinations occur between March and August each year, with the peak vaccinations occurring between March and May.

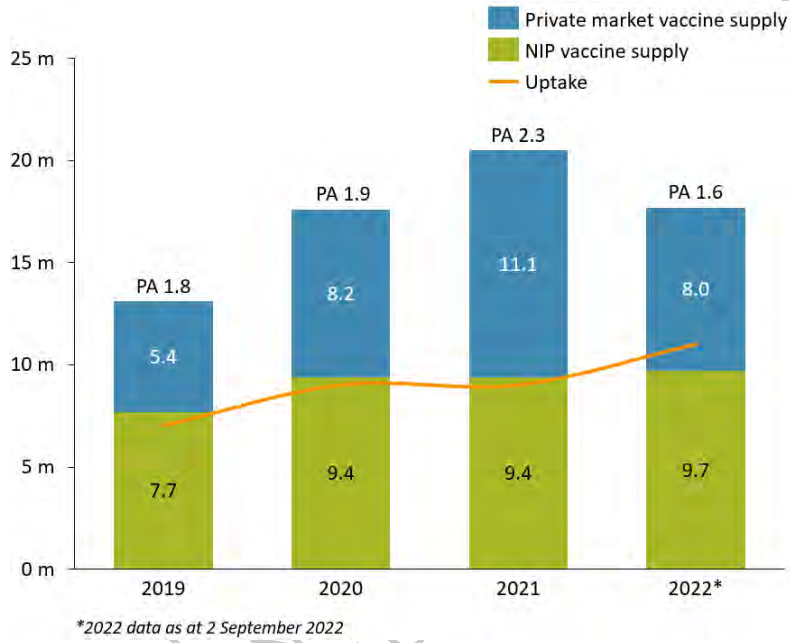


Figure 33: Influenza vaccine supply and uptake in Australia.[110]

s47C, s34(3)

[redacted]

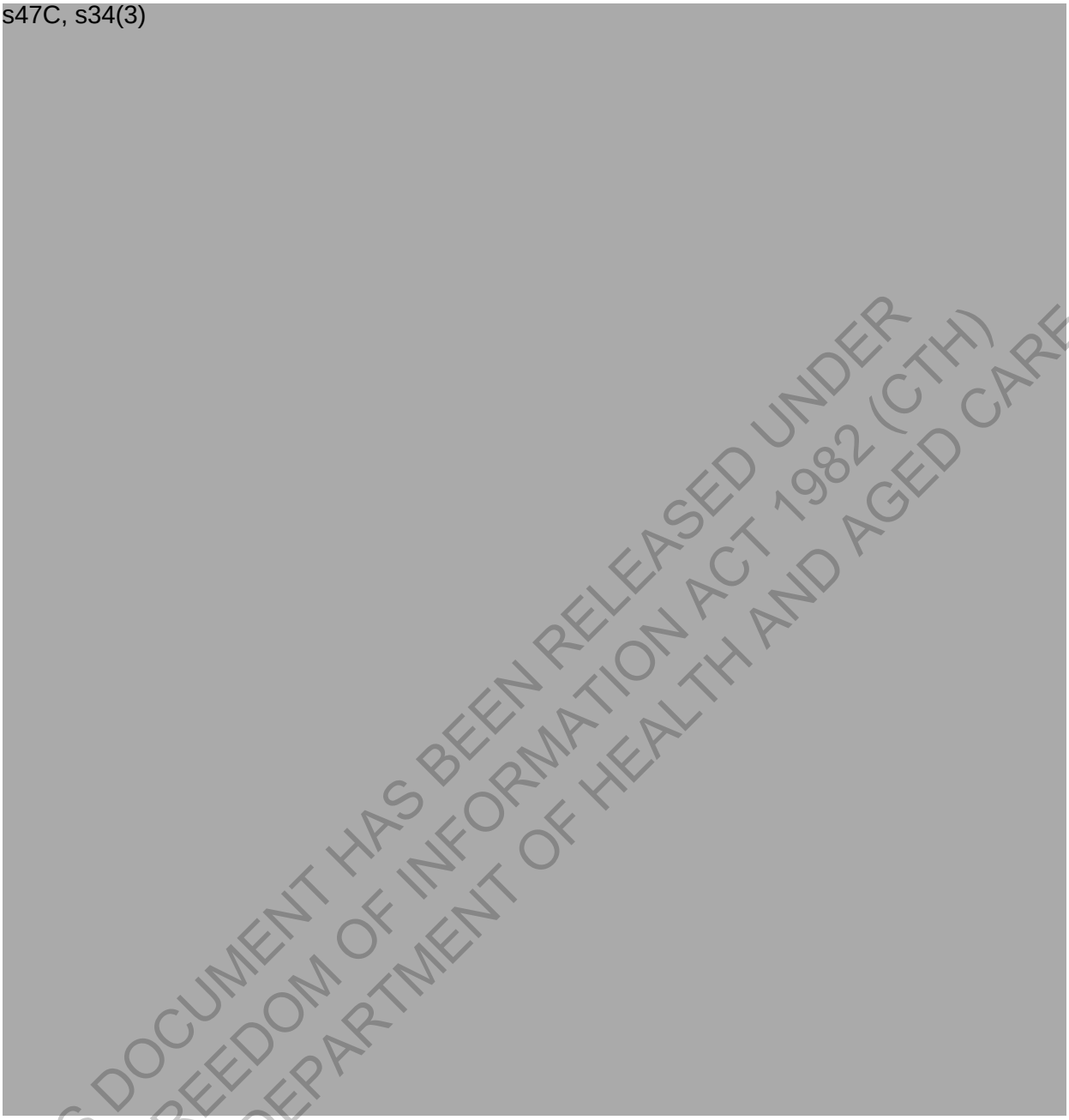
[109] Data provided in the Australian Immunisation Register (AIR) does not distinguish between private market and NIP administered vaccines.

[110] Provided by Department of Health and Aged Care, data as at 2 September 2022.

s47C, s34(3)

[redacted]

s47C, s34(3)



Minimum endemic, 'COVID-stable' quantities of effective vaccines should form the foundation of 2024 vaccines orders. In the event 'COVID-stable' has not been achieved a prudent buffer should be based on medium demand options. Specific arrangements to scale up supply in the event of high or emergency demand should be designed and implemented.

s47C, s34(3)

[112] Provided by Department of Health and Aged Care, data as at 2 September 2022.

s47C, s34(3)

Global supply of any new effective variant specific and/or broadly protective vaccines will be constrained for some time once approved by regulators. Early purchases will continue to be made in a highly competitive market. Flexible APAs are required to navigate the procurement environment and ensure adequate supplies of vaccines in Australia. Existing APAs and supply agreements provide a starting point for negotiations.

8.2 Treatments

The review has also considered a range of potential treatment demand options. Changes to the behaviour of the virus and resultant impact on infection and hospitalisation rates, will impact the need for treatments in similar manner to the uptake of vaccines. Considering the range of potential pandemic impacts, demand for COVID-19 treatments over the next few years will vary in line with the number and severity of waves of COVID-19.

s47E, s47G, s34(3)

s47C, s34(3)

The distribution of Lagevrio and Paxlovid currently occurs via the PBS with some supply through state and territory governments in the community setting. Distribution of Veklury will continue to be managed by state and territory governments through direct supply to hospitals.

[113] Provided by Department of Health and Aged Care, data as at 2 September 2022.

s47C, s34(3)

Significant stocks of treatments are available. These should provide adequate cover for the next 12 months however mechanisms to scale up supply in the event of high or emergency demand are needed.

Consideration should be given to the contractual arrangements used to secure supply treatments. In periods of low and medium demand, supply of COVID-19 treatments can be managed by sponsors through the PBS with supply responsive to demand. s47C, s34(3)

s47C, s34(3)

A proactive approach to managing engagement with sponsors is required to ensure access to treatment supplies. Regular discussions should test actual and assumed demand against the sponsors' manufacturing capacity, facilitating contingency planning in the event of a shortfall.

Ongoing monitoring of new treatments and engagement with suppliers will be needed to guarantee supply of promising emerging treatments for Australia.

Recommendation 8: *Steps should be taken, consistent with an agreed policy and risk appetite, to ensure adequate supplies of vaccines and treatments are available across 2023 and 2024 including in the event of spikes in demand. This should include additional Moderna vaccines in 2023 and, as a minimum and based on an assessment of 'COVID-19 stability', sufficient doses necessary to meet baseline demand in 2024.*

9 Conclusion

Australia's COVID-19 vaccine program has achieved high public vaccination rates by creating access to the supply of multiple safe and effective vaccine products. In addition to the vaccine coverage achieved, Australia has secured supply of therapeutic treatments for various stages of illness. In combination, the procurement, distribution, and access to vaccines and treatments have reduced the rate of mortality and hospitalisation during the COVID-19 pandemic.

The acute reactive phase of the COVID-19 pandemic has been managed through various emergency mechanisms. Despite hopeful signs, a state of 'COVID-stable' has not yet been achieved. Ongoing uncertainty in the progression of the pandemic will require continued attention to ensure a flexible approach can be continued in the medium term.

Due to changes in the virus and increased vaccination rates, most new COVID-19 infections result in a milder illness on average than was observed in previous phases of the pandemic. Research continues to quantify the long-term effects of vaccination and the effects of new products currently under development.

Critical functions of scientific and technical advisory groups will remain essential to supporting decision-making on the procurement and eligibility of COVID-19 vaccines and therapeutics based on the evidence available. Vaccines and therapeutics will likely remain a crucial part of managing the ongoing COVID-19 pandemic until 'COVID-stable' can be achieved.

The procurement of vaccines and therapeutics should be informed by an agreed risk appetite, using a portfolio and redundancy approach, to reduce deaths and hospitalisations caused by COVID-19. Vaccine and therapeutic supply and access should be designed to meet public health objectives with mitigations against wastage implemented where appropriate.

COVID-19 vaccine and therapeutic access will become a normal and ongoing function of Australian health programs when 'COVID-stable' is achieved; however, a medium-term approach which ensures vaccine and treatment access can meet the expected and potential challenges of the next two years which maintains the ability to scale up quickly will be required before business-as-usual arrangements can be entrenched.

10 Stakeholder consultation

All key stakeholders identified within the Terms of Reference were offered the opportunity to engage as part of the review process.

A broad range of stakeholders were consulted as part of the review process, including:

- Pharmaceutical Benefits Advisory Committee
- Australian Medical Association
- Australian Technical Advisory Group on Immunisation
- NSW Health
- A range of individual clinicians, pharmacists and patients
- National Pharmaceutical Services Association
- Majority of companies currently engaged to supply vaccines and/or treatments within Australia
- Therapeutic Goods Administration
- Operation COVID Shield, Office of the Coordinator General
- Department of Health and Aged Care

11 Glossary

A

Access: The ability of people in country to obtain resources for health care according to need and in a timely manner.

Adverse event: a medical reaction to receiving a vaccine or treatment. An adverse event can be very common and mild (e.g. soreness and swelling at the injection site) or severe and rare (e.g. myocarditis).

Advanced Purchasing Agreement (APA): a contractual agreement made with a supplier agreeing to buy a set amount of a product. Product is paid for upon delivery up to a set amount or cost.

Alpha: A variant of concern of SARS-CoV-2.

Ancestral: A phenotype, genotype, or gene that predominates in a natural population of organisms or strain of organisms in contrast to that of natural or laboratory mutant forms. Note: the term 'ancestral' is interchangeable with 'wild type' in the context of COVID-19.

Australian Technical Advisory Group on Immunisation (ATAGI): A technical advisory group of the Australian Government.

B

Beta: A variant of concern of SARS-CoV-2.

Bivalent vaccine: A vaccine that works by stimulating an immune response against two different variants of a virus (e.g., the Omicron and Delta variants of COVID-19).

Booster: An additional dose of a vaccine beyond the primary course, intended to increase immune protection against a disease. A COVID-19 booster is usually an individual's third dose.

C

Capacity: The ability of the Government to supply and administer vaccines and treatments, measured by the volume of product procured, the speed of product distribution, and the number of points of access for administration.

Cold-Chain: An uninterrupted and temperature-controlled supply chain network, including appropriate storage facilities, refrigerated transport, and temperature monitoring.

Cold-Chain Breach (CCB): An event whereby a product is not stored or transported within the temperature requirements intended by a cold-chain.

Commonwealth Procurement Rules (CPRs): Direct the way non-corporate Commonwealth agencies purchase goods and services and articulate the requirements for Commonwealth officials performing duties in relation to procurement. The CPRs reflect the Australian Government's policies and expectations for procuring officials.

Consumable: A physical medical tool or item which is used during a procedure. Consumables associated with vaccination include syringes and saline solution.

Coronavirus: A family of viruses which share similar characteristics and includes Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and SARS-CoV-2.

COVID-19: Coronavirus Disease 2019. The disease or illness caused by infection with the SARS-CoV-2 virus.

COVID-19 Case: An individual who has been infected with COVID-19.

COVID-Stable: The predicted future context in which COVID-19 is an endemic and low severity virus, similar to influenza, which does not require pandemic management.

Clinical Judgment: The discretion of a qualified medical professional to make decisions in the best interest of an individual's welfare, utilising existing medical advice and new clinical evidence.

D

Delta: A variant of concern of SARS-CoV-2.

Demand: The number of eligible individuals who need and want access to a vaccine or treatment.

E

Eligibility: The rules which determine if an individual is allowed to receive a vaccine or treatment.

Endemic: A disease or illness which is regularly found in a group of people or in a certain area.

F

Fixed-Schedule Distribution: An ordering and delivery model whereby participating sites receive orders of set amounts of vaccine products at regular intervals.

I

Immunocompromised: People who are immunocompromised have a reduced ability to fight infections and other diseases. ATAGI has provided a list of severely immunocompromising conditions here.

In vitro: Research undertaken outside of an entire living organism (i.e., In cells grown in the lab).

In vivo: Research undertaken within an entire, living organism (i.e., Human clinical trials).

In silico: Research undertaken using computations to predict real outcomes (i.e., simulations).

Influenza: An endemic seasonal and low severity respiratory virus.

M

Mild COVID-19: An individual with no clinical features suggestive of moderate or severe disease (more detailed definition available here).

Moderate COVID-19: A stable patient with evidence of lower respiratory tract disease (more detailed definition available here).

Monoclonal antibody (mAB): A type of treatment (composed of protein) which can bind to selected targets in the body (i.e., the spike protein of the SARS-CoV-2 virus).

Monovalent Vaccine: A vaccine that works by stimulating an immune response against one specific variant of a virus.

Morbidity: Suffering from a disease or medical condition.

Mortality: Death.

Mutation: A change in a virus's genome (genetic code). Mutations happen frequently, but only sometimes change the characteristics of a virus or organism.

Myocarditis: Inflammation around the heart. A very rare and potentially fatal side effect of COVID-19 and some vaccinations.

N

National Immunisation Program (NIP): The NIP recommends the series of immunisations given at specific times throughout your life. The immunisations range from birth through to adulthood. Vaccines listed on this program are free to all Australians provided they fall within the criteria specified in the schedule.

National Medical Stockpile (NMS): A strategic reserve of drugs, vaccines, antidotes and personal protective equipment for use in national health emergencies. The Department purchases and stockpiles these items ensuring Australia is more self-sufficient during an emergency and able to meet high levels of demand.

O

Omicron: A variant of concern of SARS-CoV-2.

On-Demand Distribution: An ordering and delivery model whereby participating sites are able to place orders for short or next day delivery to fulfill demand of expected appointments or walk-ins.

P

Pandemic: The wide and rapid spread of a new disease, often a respiratory virus. COVID-19 was declared a pandemic by the WHO on 11 March 2020 (more detail here).

Pharmaceutical Benefits Advisory Committee (PBAC): An independent statutory body to make recommendations and give advice to the Minister about which drugs and medicinal preparations should be made available as pharmaceutical benefits.

Pharmaceutical Benefits Scheme (PBS): A program of the Australian Government that subsidises prescription medication for Australian citizens and permanent residents.

Pericarditis: Inflammation around the heart. A very rare and potentially fatal side effect of COVID-19 and some vaccinations.

Portfolio Approach: A procurement approach whereby a number of different products are procured in order to reduce risk or increase choice.

Post-exposure prophylaxis: A medicine taken to prevent being infected with a specific disease (e.g., COVID-19) after exposure (e.g., a known household contact).

Pre-exposure prophylaxis: A medicine taken pre-emptively to prevent infection with a specific disease (e.g., COVID-19) where there is a high risk of exposure.

Primary course: An initial course of vaccination to provide initial protection. A primary course of COVID-19 vaccination is usually two doses (full ATAGI guidance on a primary course is available here).

Procurement: The process of purchasing and acquiring vaccines for immunisation against COVID-19.

Purchase Administration ratio (PA ratio): The number of doses required to be purchased to meet the forecasted vaccines administrations

Q

Quarantine: A period of isolation to prevent the spread of infection illnesses or diseases.

S

SARS-CoV-2: Severe Acute Respiratory Syndrome (SARS) Coronavirus (CoV) 2. The virus that causes COVID-19.

Severe COVID-19: A patient with signs of moderate disease who is deteriorating (more detailed definition available here).

Science and Industry Technical Advisory Group (SITAG): A committee that provides advice to the Australian Government on the purchasing and manufacturing of COVID-19 treatments and vaccines.

Sponsor: The person or company responsible for exporting or importing therapeutic goods into Australia, manufacturing therapeutic goods in Australia, or arranging another party to import, export, or manufacture therapeutic goods (see more here).

Sub-variant: A variant of SARS-CoV-2 which is closely related to another variant and behaves in a similar manner.

Supply: The quantity of a particular product (i.e., vaccines, consumables) available to consumers.

T

Therapeutic Goods Administration (TGA): The medicine and therapeutic regulatory agency of the Australian Government.

TGA provisional approval: Provisional approval allows a promising treatment to be used in Australia for a limited period for a serious or life-threatening condition, which has lesser research and information on the medicine than that required by the TGA for approval of a standard prescription medicine.

TGA provisional determination: The granting of a provisional determination means that the TGA has decided that relevant sponsors are eligible to apply for provisional registration/approval for the vaccine in the Australian Register of Therapeutic Goods (ARTG) within 6 months.

Therapeutic: A medicine, treatment, or drug. Note: the term 'therapeutics' is interchangeable with 'treatments' in the context of COVID-19.

Treatment: The use of an agent, procedure, or regimen, such as a drug, surgery, or exercise, to cure or mitigate a disease, condition, or injury. Note: the term 'therapeutics' is interchangeable with 'treatments' in the context of COVID-19.

V

Vaccine: Medicines which induce immunity to prevent people being infected with specific diseases such as COVID-19.

Vaccine Administration Error (VAE): A clinical error in the administration of a vaccine product (e.g., administering an incorrect dosage or administering a dose outside a set schedule).

Vaccine Effectiveness (VE): The degree to which a vaccine performs in the real world.

Vaccine Efficacy: The degree to which a vaccine prevents disease, and possibly also transmission, under ideal and controlled clinical trial circumstances (i.e., comparing a vaccinated group with a placebo group).

Variant: A viral genome (genetic code) that may contain one or more mutations which differ from the wild type/ancestral virus.

Variant of concern: A variant of SARS-CoV-2, identified by the WHO, with a potential to be more infectious or cause more severe illness than the ancestral variant. More information on the WHO variant tracking is available here.

Virus: A small infectious particle that can cause disease in humans and other animals.

Virus neutralising antibody: An antibody that binds to a virus (e.g., SARS-CoV-2) and interferes with its ability to infect a cell.

W

Wastage: Product that is procured by not used due to expiry or damage.

Wild type: A phenotype, genotype, or gene that predominates in a natural population of organisms or strain of organisms in contrast to that of natural or laboratory mutant forms. Note: the term 'ancestral' is interchangeable with 'wild type' in the context of COVID-19.

Winter dose: Now referred to as a 'fourth dose'. An additional booster dose recommended for certain cohorts in preparation for a predicted winter spike in infections in 2022.

Attachment 1: Terms of Reference

Australian Government

Department of Health and Aged Care

Terms of Reference

COVID-19 Vaccines and Treatments purchasing and procurement review

Purpose

The Australian Government is seeking an independent review of COVID-19 vaccine and treatment purchases and associated processes over the course of the COVID-19 pandemic, inclusive of examining the state of supply currently and over the next 12-24 months.

Scope of work

- **Examine previous procurement approaches to COVID-19 vaccines and treatments and assess their efficacy in delivering:**
  - **sufficient and timely supply;**
  - **appropriate regulatory oversight of safety and efficacy;**
  - **value for money; and**
  - **appropriate mitigation of risks.**
- **Examine the currently procured and contracted supply of COVID vaccines and treatments and assess the state of supply and management of over-supply.**
- **Examine Australia's current procurement processes for COVID-19 vaccines and treatments, assessment processes for future purchases, the state of current international vaccine market and appropriate management of future purchasing risk.**
- **Compare Australia's purchasing and procurement processes with similar jurisdictions.**
- **Make recommendations on future vaccine distribution including the suitability of distribution processes to meet future booster programs.**
- **Make recommendations on future procurement strategy mindful of the latest medical advice and state of international supply over the medium term.**
- **Any other matters relevant to vaccine and treatment procurement related to the above.**

Out of scope

- Matters related to broader pandemic preparedness.
- Pandemic preparedness purchases and deployments of other medical interventions through the National Medical Stockpile.

Timeline

- Preliminary findings to be provided to the Minister for Health and Aged Care within four weeks of commencement of engagement.
- Final report and recommendations provided to the Minister for Health and Aged Care by 31 August 2022.

Deliverables

- Preliminary Findings
- Final Report

Governance

The review is to report to the Minister for Health and Aged Care, Minister Butler by 31 August 2022.

The review will be led by Jane Halton.

The review will be supported by Department of Health and Aged Care, key internal stakeholders include:

- Brendan Murphy, Secretary (and Chair of the Scientific and Technical Advisory Group – (SITAG)).
- Penny Shakespeare, Deputy Secretary.
- John Skerritt, Deputy Secretary, Therapeutic Goods Administration.
- Paul Kelly, Chief Medical Officer (and Deputy Chair of SITAG).
- Trish Garrett, First Assistant Secretary, Vaccine Operations and Data Division.
- Adriana Platona, First Assistant Secretary, Technology Assessments and Access Division.

Consultations

Vaccine manufacturers: Pfizer, Moderna, Novavax, AstraZeneca.

COVID-19 treatment manufacturers: GSK, Roche, AstraZeneca, Pfizer, MSD, Gilead.

Professor Andrew Wilson, Chair, Pharmaceutical Benefits Advisory Committee.

Associate Professor Nigel Crawford, Chair, Australian Technical Advisory Group on Immunisation.

Attachment 2: SARS-CoV-2 Science

SARS-CoV-2 is a novel coronavirus first identified in Wuhan, China in late 2019.

SARS-CoV-2 replicates mostly in the upper respiratory tract (see Figure 1). This explains most of the respiratory symptoms associated with COVID-19 illness, as well as the methods of transmission, which occurs mainly through respiratory particles made up of droplets and aerosols.[1] The reproductive rate (R0) of SARS-CoV-2, or the number of individuals that one patient may pass the virus to when first introduced into a population who have no immunity, has been estimated at around 3, but subsequent strains (and especially Omicron) have been more transmissible.[2] Infected individuals who are asymptomatic (not presenting signs of infection) have similar viral loads to symptomatic patients, indicating that transmission can still occur from people with no symptoms but those with symptoms (e.g., cough) appear to spread the virus more often.[3]

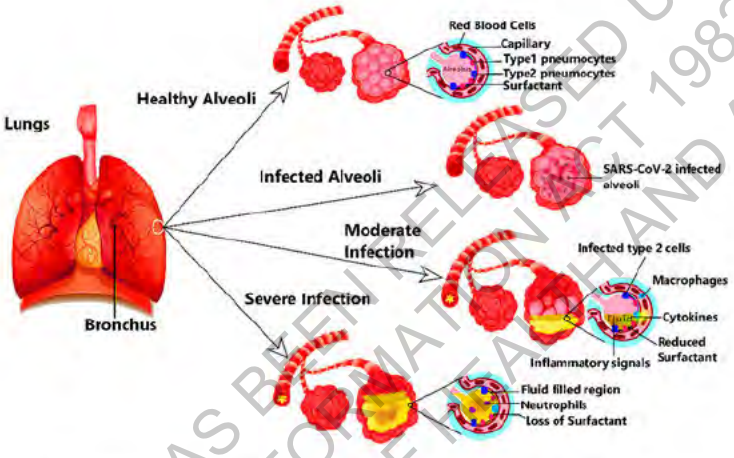


Figure 1: A diagram of human lungs, showing the effect of COVID-19 illness caused by infection with SARS-COV-2 in the alveoli (microstructures of the lung which pass oxygen into the blood).[4]

Strict control measures were introduced by nearly all countries, with intent to slow infection rates due to the highly transmissible nature of this disease. Since the first case of COVID-19 was identified in Australia in early 2020, over 9 million cases have been reported, mostly in 2022.[5] Most of these cases are now locally acquired indicating high levels of transmission within the community after the virus entered the country. Various Government controls and interventions have been implemented over the course of the pandemic since March 2020, to limit the spread of the virus, including mask mandates, border and travel restrictions, controls on crowded indoor venues, and vaccine requirements. Many of these interventions were successful at reducing infection rates.

Emerging complications from COVID-19 illness, which are still being investigated, include reinfection and the persistence of symptoms more than 3 months following infection called "Long Covid". Cases

[1] L Zou et al., 'SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients', *NEJM*, 2020, Vol. 382.
[2] Y Liu et al., 'The reproductive number of the Delta variant of SARS-CoV-2 is far higher compared to the ancestral SARS-CoV-2 virus', *Journal of Travel Medicine*, 2021, Vol. 28, No. 7.
[3] L Zou et al., 2020
[4] V Kumar et al., 'COVID-19 pandemic: mechanism, diagnosis, and treatment', *Chemical Technology and Biotechnology*, 2020, Vol. 96, pp. 299-308.
[5] Australian Government, 'Coronavirus (COVID-19) case numbers and statistics', *Department of Health and Aged Care*, 4 August 2022, accessed 10 August 2022.

of reinfection were first reported in August 2020 and have now cumulatively become more common. Reinfection appears to be associated with less severe disease and has a 90 percent lower chance of hospitalisation or mortality compared to initial infections.[6] Numerous studies now show that antibodies which provide immune protection from COVID-19 may decay rapidly following infection or drop significantly from the initial peak response.[7] Waning antibody immunity in the months following infection allows for additional infections to occur. However, T Cell immunity appears to persist at least 12 months following infection which protects against serious illness or death.[8] Initial research also suggests that vaccination along with hybrid immunity may be key to decreasing the risk of re-infection with COVID-19.[9]

Studies have also noted instances of persistent COVID-19 where patients who are immunocompromised can remain infected for up to 150 days.[10] COVID-19 infection in the gastro-intestinal tract has also been documented in non-immunocompromised individuals but is not thought to be related ongoing viable virus and thus spreading COVID-19. Approximately 13 percent of asymptomatic individuals still test positive for faecal viral shedding of COVID-19 genetic material four months after their initial infection, despite testing negative via nasal swabs.[11]

A long-term study of patients in the UK found that 9.8 percent reported at least one symptom at 12 weeks following infection.[12] The largest study to date found that about 3.7% of people developed long COVID, when defined as experiencing one or more of the three symptom clusters three months after infection. It was estimated that the median duration of long COVID of 3.99 months (IQR 3.84–4.20) in community infections, while hospitalized cases were estimated to experience a longer median duration of 8.84 months (IQR 8.10–9.78). Among COVID patients who develop long COVID in 2020 and 2021, 15.1% (10.3–21.1) continued to have persistent symptoms at 12 months after COVID infection. This implies that if 6% of people infected have long Covid at 12 weeks that about 1% of those infected might still have long covid symptoms at 12 months (15% of 6%).

While the mechanism by which cases of Long COVID causes symptoms is not yet understood, there is a concern it will result in an increased burden of disease on infected individuals and efforts are underway to determine potential therapeutic approaches for treatment.[13] Research is yet to quantify the full effects of vaccines on managing the long-term impacts of COVID-19. Some studies suggest that up to 40 percent of individuals may experience some form of persistent COVID-19 symptoms (such as fatigue, cough, pain or "brain fog") 12 weeks following infection and further investigation is required to determine the true incidence of cases due to the number of unreported cases.[14] Initial research suggests that vaccination may be key to decreasing the risk of re-infection

[6] L Abu-Raddad et al., 'Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections.', *NEJM*, 2021, Vol. 385.
[7] A Babiker et al., 'The Importance and Challenges of Identifying SARS-CoV-2 Reinfections', *Virology*, 2021, Vol. 59., 4, s.l
[8] L Guo et al., 'SARS-CoV-2-specific antibody and T-cell responses 1 year after infection in people recovered from COVID-19: a longitudinal cohort study', *The Lancet Microbe*, 2022, Vol. 3, pp. 348-356
[9] AM Cavanaugh et al., 'Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May–June 2021', *Morbidity and Mortality Weekly Report*, 2021 Vol. 70, pp. 1081-1083.
[10] P Doherty, 'Issue #115: Persistence of SARS-CoV-2 and Long COVID, 3 - The inside/outside of us', *Doherty Institute*, 01 August 2022, accessed 11 August 2022.
[11] P Doherty, 1 August 2022,
[12] D Ayoubkhani et al., 'Update on long COVID prevalence estimate', *UK Government Publishing Service,* 01 February 2021, accessed 19 August 2022.
[13] B Jarrott et al., '"LONG COVID"—A hypothesis for understanding the biological basis and pharmacological treatment strategy', *Pharmacology Research Perspectives*, 2022, Vol. 10.
[14] B Jarrott et al., 2022

with COVID-19 and that vaccinated patients also report improvement in the symptoms of Long COVID compared to unvaccinated patients.[15]

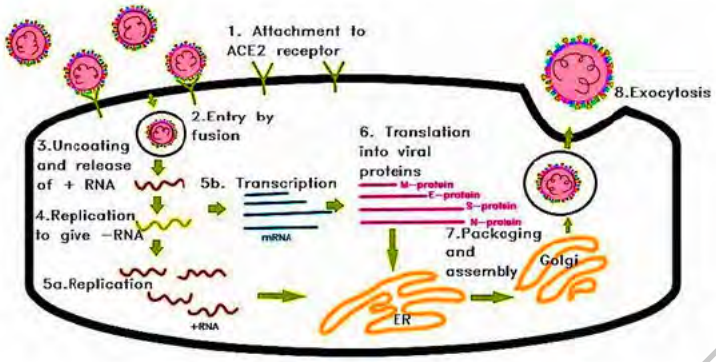


Figure 2: The mechanism of SARS-CoV-2 reproduction in a host cell, starting from attachment of the virus onto ACE2 receptors on the outside of the cell, replication of the virus' genetic material, assembly of the proteins encoded in that viral genetic material into a new copy of the virus and the export (exocytosis) of new viral particles into the body. Each virus can result in the production of many new viruses.[16]

Since the emergence of COVID-19, the highly infectious virus has undergone multiple mutations resulting in changes to its behaviour which affects its transmission rate and associated mortality and morbidity. Mutations to the genetic code of the virus occur naturally and randomly during the process of replicating within an infected host (see Figure 2) and the mutated virus can then be transmitted between individuals.[17] Although the virus is not able to mutate when it is outside of a host, persistent infection in a host may allow the virus to accumulate multiple mutations or recombine with other viruses within the same host to produce highly mutated variants which differ in a substantial way and is considered as a new lineage or family of the virus.[18] Initial research indicates that immunocompromised individuals with persistent COVID-19 infections may be an important driver for the emergence of these new variants at higher rates than expected for viruses, highlighting another reason for protecting more vulnerable members of the community from COVID-19.[19]

Of the variants which have naturally emerged since SARS-CoV-2 was first identified in 2019, the World Health Organisation (WHO) has labelled several as Variants of Concern (VOCs) in response to increased transmissibility, increased severity of disease, or reduced neutralisation by the immune system.[20] These variants have been assigned Greek letter names to assist in monitoring and reporting (see Figure 3). Many of the mutations present in VOCs have occurred in the genetic code for the spike protein which is the main target of neutralising anti-bodies (made by the body in response to infection or vaccination).[21] Mutations of this protein often result in increased immune escape, or a decreased efficacy of anti-bodies to bind to and destroy the virus. This results in increased rates of transmission or illness as the virus avoids the immune system and replicates at

[15] A Mumtaz et al., 'COVID-19 Vaccine and Long COVID: A Scoping Review', *Life*, 2022, Vol. 12.
[16] V Kumar et al., 'COVID-19 pandemic: mechanism, diagnosis, and treatment', *Chemical Technology and Biotechnology*, 2020, Vol. 96, pp. 299-308.
[17] K Tao et al., 'The biological and clinical significance of emerging SARS-CoV-2 variants', *Nature Reviews Genetics*, 2021, Vol. 22, pp. 757–773.
[18] K Tao et al., 2021
[19] K Kupferschmidt, 'As Omicron rages on, scientists have no idea what comes next', *Science*, 2022, Vol. 377.
[20] WHO. 'Tracking SARS-CoV-2 variants', *WHO,* 2 August 2022, accessed August 9, 2022.
[21] K Tao et al., *The biological and clinical significance of emerging SARS-CoV-2 variants. 2021*, Nature Reviews Genetics, Vol. 22, pp. 757–773.

greater rates. The higher rates of transmission from these VOCs makes each new variant more biologically competitive and allows the new variant to replace older variants.

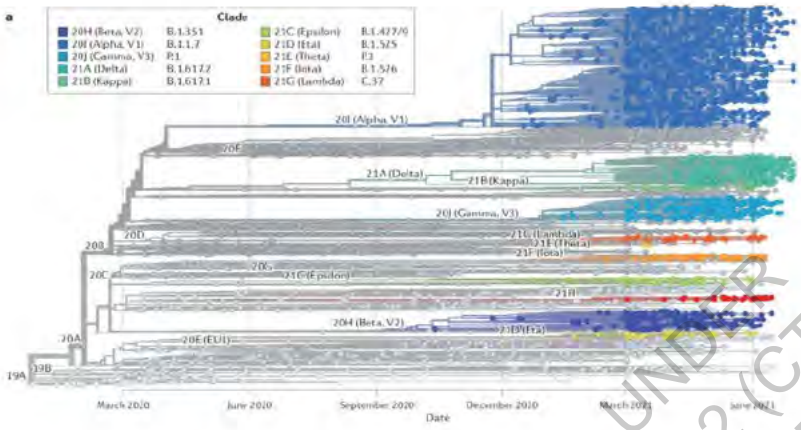


Figure 3: Phylogenetic tree showing the creation of SARS-CoV-2 variants via lineages of mutation between early 2020 and June 2021.[22]

In Australia, the ancestral or wild type SARS-CoV-2 strain was overtaken by new variants with increased viral fitness, and immune evasion, as they emerged from various other countries (see Figure 4).[23] The dominant variants that produced new waves of infection in Australia include Alpha (which was approximately 50 percent more transmissible than the ancestral strain and caused an estimated 50 percent increase in mortality in the UK) and Delta (which developed additional spike protein mutations allowing it to cause breakthrough infections in previous infected or vaccinated individuals and had a much higher reproductive rate causing more severe illness).[24]

The current dominant VOC in August 2022 is the Omicron BA.5 variant. Because it has spread so rapidly, the Omicron variant has been able to mutate more rapidly resulting in the presence of multiple sub-variants, including BA.1, BA.2, BA.3, BA.4, and BA.5.[25] While each sub-variant has slightly different characteristics, particular concern surrounds the BA.2, BA.4, and BA.5 sub-variants due to their increased ability for immune escape even in vaccinated individuals but has not resulted in increased deaths or hospitalisation in vaccinated people.[26]

[22] K Tao et al., 2021

[23] JE Bowen et al., 'Omicron spike function and neutralizing activity elicited by a comprehensive panel of vaccines' *Science*. July 2022.

[24] P Mlcochoba et al., 'SARS-CoV-2 B.1.617.2 Delta variant emergence and vaccine breakthrough', *Nature Portfolio*, 2021.

[25] S Duchene and A Porter, 'Why are there so many new Omicron sub-variants, like BA.4 and BA.5? Will I be reinfected? Is the virus mutating faster?' [Online] *Doherty Institute*, 06 May 2022, accessed 09 August 2022.

[26] S Duchene and A Porter, 06 May 2022

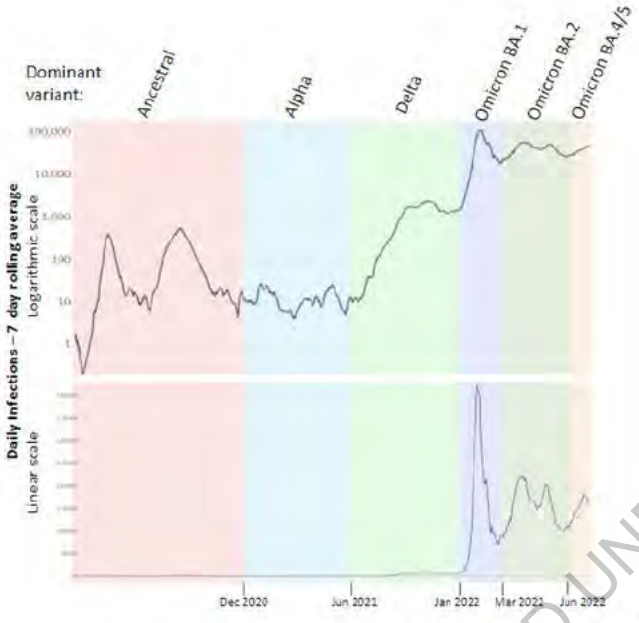


Figure 4: Australian daily COVID-19 infections by dominant SARS-CoV-2 variant.[27]

Researchers suggest that new sub-variants will continue to emerge and drive new infections.[28] In addition, the presence of multiple SARS-CoV-2 variants within a population gives rise to the risk of recombination events, where two distinct variants or sub-variants can infect an individual at the same time and swap their genetic material, resulting in a new variant which contains traits from each of the two parent strains.[29] A recombination event like this has not resulted in a major new wave in any country. As it is not possible to predict the further evolution of the virus, scientists continue to monitor mutations and recombination events to predict virus behaviours, suggest measures to reduce the spread of variants and sub-variants, and guide the development of vaccines and therapeutics.

Historically, respiratory viruses which have emerged and resulted in severe pandemics have evolved over time to become a mild and seasonal virus. This was the case with the 1918 "Spanish Flu" pandemic which is the ancestor of most modern influenza A viruses and became endemic due to ongoing high rates of infection but lower fatality rates. A survey conducted by Nature indicated that 89 of the 100 immunologists, infectious-disease researchers, and virologists believe that SARS-CoV-2 will also become an endemic virus.[30] This would result in a COVID-stable environment, where the behaviour of the virus will be easier to predict, and the risk of severe illness and mortality would be greatly reduced.

The current unpredictable nature of the SARS-CoV-2 virus will require ongoing monitoring and control interventions until COVID-stable can be achieve. This would result in a COVID-stable environment, where the behaviour of the virus will be easier to predict, and on a population basis, the risk of severe illness and mortality would be greatly reduced. However, the current unpredictable nature of the SARS-CoV-2 virus will require ongoing monitoring and control interventions until COVID-stable can be achieve.

[27] Our World in Data, 'Coronavirus (COVID-19) Cases', *Our World in Data*, 22 July 2022, accessed 22 July 2022.
[28] K Kupferschmidt, 'As Omicron rages on, scientists have no idea what comes next', *Science*, 2022, Vol. 377.
[29] S Duchene and A Porter, 6 May 2022.
[30] K Kupferschmidt, 2022.

Attachment 3: Global Economic and Policy Response

Impact on Australian Economy

COVID-19 has a significant impact on the Australian and state and territory economies in the initial phases of the outbreak. Once states and territories adopted national advice regarding physical distancing and business closures, demand for goods and services slowed significantly (see Table A below). Australia's demand for goods and services shrunk by 7.4%, headlined by New South Wales and Victoria recording contractions of 8.6% and 8.5% respectively in June 2020. Australia also fell into a technical recession during this period.

Jurisdiction /Quarter	VIC	NSW	QLD	SA	WA	NT	ACT	TAS	ALL
Dec '19	-0.1	0.5	0.2	-0.2	-0.2	0.3	0.8	-1	0.1
Mar '20	-0.1	-1.5	-0.3	-1	0.9	-1.2	2.1	0.6	-0.5
June '20	-8.5	-8.6	-5.9	-5.8	-6	-4.9	-2.2	-7.4	-7.4

Table 1: State final demand, quarterly volumes seasonally adjusted. [1]

Over 1 million Australians were unemployed in this period and 3.8 million Australians accessed JobKeeper support. To combat the reduced demand in Australia, both federal, state and territory governments provided unprecedented economic support to assist individuals and businesses hit by the pandemic.

Jurisdiction	VIC	NSW	QLD	SA	WA	NT	ACT	TAS	ALL
Support (AU$ million)	44 000	53 000	14 200	4 000	11 200	400	475	1 500	**3 430 000**

Table 2: Economic stimulus provided by jurisdiction.[2]

Economies began to recover but there was another contraction in the September '21 quarter caused by the Delta lockdowns in Sydney and Melbourne (see Figure 1).

[1] Australian Bureau of Statistics, 'Australian National Accounts: National Income, Expenditure and Product, December 2019', *Australian Bureau of Statistics,* 4 March 2020, accessed 18 August 2022 and Australian Bureau of Statistics, 'Australian National Accounts: National Income, Expenditure and Product, March 2020', *Australian Bureau of Statistics,* 3 June 2020, accessed 18 August 2022 and Australian Bureau of Statistics, 'Australian National Accounts: National Income, Expenditure and Product, June 2020', *Australian Bureau of Statistics,* 3 June 2020, accessed 18 August 2022.

[2] Victorian Government, 'Budget Speech', *Department of Treasury and Finance Victoria,* 2 May 2022, accessed 19 August 2022; New South Wales Government, 'Budget Speech', *New South Wales Government,* 21 June 2022, accessed 19 August 2022; Queensland Government, 'Queensland's economic recovery plan', *COVID-19 Queensland,* 18 July 2022, accessed 19 August 2022; Government of South Australia, '2021-22 Budget Speech', *Department of Treasury and Finance South Australia*, 22 June 2021, accessed 19 August 2022; Government of Western Australia, 'Budget Paper No. 1 Budget Speech', *Our State Budget*, 12 May 2022, accessed 19 August 2022; Northern Territory Government, 'Budget Paper No. 1 Speech and Appropriation Bill', *Northern Territory Treasury,* 10 November 2020, accessed 19 August 2022; Australian Capital Territory Government, 'Budget Speech', *Treasury ACT,* 31 August 2021, accessed 19 August 2022; Tasmanian Government, '2022-23 Budget Speech', *Tasmania Treasury,* 26 May 2022, accessed 19 August 2022; and Australian Government, 'Budget overview', *Budget 2022,* 29 March 2022, accessed 19 August 2022.

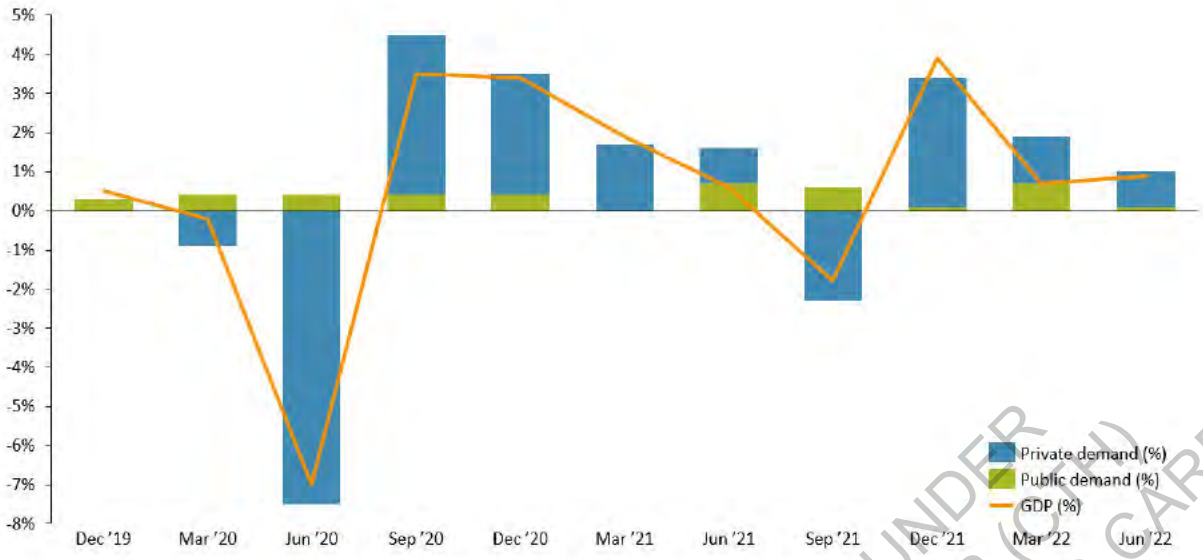


Figure 1: Australia public and private demand, quarterly volumes seasonally adjusted.[3]

Comparison of International Responses to COVID-19

Nine countries were identified as comparison countries for this report. The below tables consider the vaccine manufacturing capacity, APAs negotiated, market interventions, vaccination program design and other policy settings implemented.

Global Market Interventions

Throughout COVID-19 the supply of vaccines waned due to shortage of raw materials and labour. To combat this, certain countries intervened in the vaccine market to ensure supply was guaranteed for their citizens. Then United States (US) President Donald Trump signed an executive order to ensure vaccines were prioritised for American citizens, effectively stopping exports. France, as a member of the EU (European Union), was a part of the EU's vaccine export mechanism, which allowed the EU to block exports of shipments. Notably, this occurred when Italy blocked a shipment of AstraZeneca into Australia in 2021. Other countries such as the United Kingdom built in clauses in contracts which ensured that manufacturers provided vaccines to the UK prior to other countries.

Australia	United States	United Kingdom	Canada	Israel
No	Yes	Yes, through commercial contracts	No	No

Japan	Singapore	Norway	France	New Zealand
No	No	No	Yes (EU)	No

Table 3: Market interventions imposed by comparable country.

[3] Australian Bureau of Statistics, 'Australian National Accounts: National Income, Expenditure and Product, June 2022', *Australian Bureau of Statistics,* 7 September 2022, accessed 16 September 2022.

Manufacturing Capacity

Most countries in the comparison group can manufacture vaccines at on shore production facilities. Australia contracted CSL to produce AstraZeneca's vaccine. Australia has also followed the lead from Canada, who have begun establishing mRNA vaccine facilities following the emergence of COVID-19. Countries such as the United Kingdom and Singapore have heavily invested into vaccine research and manufacturing prior to the coronavirus outbreak, with the UK investing £66m into their Vaccine Manufacturing Innovation Centre (VMIC). France, being home to one of the largest pharmaceutical companies Sanofi can export approximately 85% of their production.

Australia	United States	United Kingdom	Canada	Israel
Yes	Yes	Yes	Built during pandemic	No

Japan	Singapore	Norway	France	New Zealand
Yes	Yes	No	Yes	Partial Production only

Table 4: Vaccine manufacturing capacity by comparable country.

Negotiation of APAs

Each country was responsible for sourcing and financing vaccines for its citizens. Some regions, such as the EU, utilised group purchasing agreements in order to secure supply and allow for equitable distribution. Available data on the number and cost of doses differs per country. A summary of the purchases of comparable countries is provided below (see Table 5).

	Australia[3]	United States[4]	United Kingdom[4]	Canada[6]	Israel[4]
Total doses	254.8 million	3.4 billion	588 million	714.9 million	70.7 million
Total cost	AUD $8 billion	n/a	£5.8 billion	CAD $9 billion	SD $788 million

	Japan[7]	Singapore[8]	Norway[9]	France[10]	New Zealand[5]
Total doses	842 million	n/a	n/a	n/a	38 million
Total cost	JPY 2.4 trillion	n/a	EU Purchasing Agreement	EU Purchasing Agreement	NZ $964.3 million

Table 5: Total doses purchased and total cost of procurement by country.

Channels used to administer vaccines

During the associated vaccine rollout, most countries implemented the use of mass vaccination hubs in locations such as unused athletic arenas, stadiums, and unused warehouses. Allowing for central points of presence to help with logistics. As the rollout became more advanced, several additional avenues opened, with GPs (General Practitioners) and medical centres offering vaccinations and mobile vaccinations along with "pop-up" clinics opening in key areas where the vaccination rate was low.

Australia	United States	United Kingdom	Canada	Israel
Mass Vaccination Hubs	Mass Vaccination Hubs	Mass Vaccination Hubs	Mass Vaccination Hubs	Mass Vaccination Hubs
Pharmacies	Pharmacies	Pharmacies	Pharmacies	Medical Centres
General Practices	General Practices	General Practices	General Practices	Pop-up Clinics
Retail Shops	Retail Shops	Medical Centres	Medical Centres	Mobile Vaccination
Pop-up Clinics	Pop-up Clinics	Pop-up Clinics	Pop-up Clinics	Workplace Vaccination
Medical Centres	Medical Centres	Mobile Vaccination	Mobile Vaccination	
Mobile Vaccination			Workplace Vaccination	

Japan	Singapore	Norway	France	New Zealand
Mass Vaccination Hubs	Mass Vaccination Hubs	Mass Vaccination Hubs	Mass Vaccination Hubs	Mass Vaccination Hubs
Universities	Mobile Vaccination		Medical Centres	Mobile Vaccination
Workplaces	Medical Centres		General Practices	General Practices
Pop-up Clinics			Pop-up Clinics	Pharmacies
Medical Centres			Sports Stadiums	Drive-through vaccination hubs

Table 6: Site types used to administer COVID-19 vaccines by country.

Mask mandates and stay at home policies

Most countries imposed various measures to control the spread of COVID-19, with all comparable countries (excluding Japan) imposing mask mandates throughout points of the pandemic. The US and Canada, much like Australia, delegated mask rules to the states and territory to police and establish. Australian states followed advice from AHPPC regarding mask usage. Like mask mandates,

[4] Australian Government, 'Australia's vaccine agreements', *Department of Health and Aged Care, 08* July 2022, accessed 10 August 2022.
[5] UNICEF, 'COVID-19 Vaccine Market Dashboard', *UNICEF,* accessed 10 August 2022.
[6] New Zealand Government, 'Budget at a Glance 2021', The Treasury, 20 May 2021, accessed 10 August 2022 and L Malpass, 'Budget 2021: Covid-19 vaccine programme revealed to cost $1.4 billion', *Stuff.co.nz,* 19 May 2021, accessed 10 August 2022.
[7] Government of Canada, 'Procuring vaccines for COVID-19', *Government of Canada,* 24 Feb 2022, accessed 10 August 2022.
[8] Japan Times, 'Japan urged to consider cost-effectiveness of vaccinations', *Japan Times,* 14 April 2022, accessed 10 August 2022.
[9] Singapore Government, 'COIVD-19 Vaccination', *Ministry of Health Singapore*, 22 July 2022, accessed 10 August 2022.
[10] I Skjesol and J Q Tritter, 'The Norwegian way: COVID-19 vaccination policy and practice', *Science Direct*, June 2022, accessed 10 August 2022, France.
[11] Ministere De L'Europe et des affaires etrangeres, 'France, a major player in vaccine solidarity', *France Diplomacy,* February 2022, accessed 10 August 2022.

most countries-imposed lockdowns throughout the pandemic. Japan, again being the exception to the rule, did not impose these orders, much like Singapore. Instead, these countries just recommended not leaving home unless appropriate. It is important to note that in some Asian countries, such as Japan, wearing masks in public places and during flu season is common practice.

Country	Mask Mandated at any time?
Australia	Yes – state discretion, federally imposed on travel
United States	Yes – state discretion, federally imposed on travel
United Kingdom	Yes
Canada	Yes – state discretion, federally imposed on travel
Israel	Yes
Japan	No
Singapore	Yes
Norway	Yes – state discretion
France	Yes

Table 7: Imposed mask mandate by comparable country

Country	Lockdown/Stay at home orders
Australia	Yes – state declaration
United States	Yes – state autonomy and declarations
United Kingdom	Yes
Canada	Yes
Israel	Yes
Japan	No
Singapore	No
Norway	Yes
France	Yes

Table 8: Stay at home/lockdown orders by comparable country

Attachment 4: Vaccines

Vaccines are generally administered in the upper arm of a patient and use a syringe to deliver the active part of the vaccine into muscle where it can interact with the immune system.[1] In addition to their varied mechanisms of action, each of the vaccines also has a different efficacy and safety profile which has been considered by regulators. Common side effects expected following vaccination include pain, swelling, fever and headaches. Serious side effects or adverse events can also occur and may vary in frequency in different populations.[2] In Australia, side effects and adverse events related to the COVID-19 vaccine products are monitored and reported by the TGA on a regular basis as part of post-market surveillance activities.

AstraZeneca

Vaxzevria (AstraZeneca), developed by Oxford University researchers, is a viral vector vaccine. It is comprised of modified version of a virus which cannot replicate in the patient and triggers the production of the SARS-CoV2 spike protein from a DNA template to train the immune system to identify and kill the virus.[3] A single dose of the Vaxveria (AstraZeneca) vaccine was found to be 94 percent effective against COVID-19 hospitalisations from the Alpha variant.[4] In the months following the commencement of vaccination with the Vaxzevria (AstraZeneca) viral vector vaccine, incidences of a serious blood clotting disorder known as Thrombosis with Thrombocytopenia Syndrome (TSS) were identified in patients vaccinated with this vaccine.[5] The rate of TTS following vaccination with Vaxzevria (AstraZeneca) was found affect 2 in every 100,000 individuals after a first dose or 0.3 in every 100,000 following a second dose and was more common in younger women.[6] Due to the increased risk of TTS, ATAGI guidance was updated throughout the pandemic to balance the risk of side effects, the benefits of vaccination against COVID-19, the age of the recipient, and the availability of other vaccines. ATAGI's current guidelines recommend that alternate vaccine products should be used in those aged 16 to 60 years of age where possible but stressed that the benefits of vaccination with this product outweighed the very low risk of TTS, especially for those aged 60 years and above.[7]

Pfizer and Moderna

Comirnaty (Pfizer) and Spikevax (Moderna) are mRNA vaccines. They are comprised of a manufactured chain of genetic material which is used as a template for the body to build copies of the SARS-CoV-2 spike protein to train the immune system. During the Alpha wave, efficacy of the Comirnaty (Pfizer) vaccine against hospitalisation was found to be 95 percent following the two-dose schedule,[8] and the Spikevax (Moderna) vaccine was found to have an efficacy of 80 percent after two doses.[9] Against the Delta variant, the efficacy against hospitalisation by Comirnaty (Pfizer) is 96

[1] P Doherty, 'Issue #84: Viruses, Vaccines and COVID-19: arming up', *Doherty Institute*, 22 November 2021, accessed 11 August 2022.
[2] P Anand and V Stahel, 'The safety of Covid-19 mRNA vaccines: a review', *Patient Safety in Surgery*, 2021, Vol. 15.
[3] P Doherty, 22 November 2021
[4] E Vasileiou et al., 'Effectiveness of first Dose of COVID-19 vaccines against hospital admissions in Scotland: national prospective cohort study of 5.4 million people', *The Lancet,* preprint, 2021,
[5] SF Gordon et al., **'**Immune thrombocytopenia following immunisation with Vaxzevria ChadOx1-S (AstraZeneca) vaccine, Victoria, Australia*', Vaccine*, 2021, Vol. 39, pp. 7052-7057.
[6] TGA, **'**COVID-19 vaccine safety report - 28-07-2022', *TGA*, 28 July 2022, 11 August 2022.
[7] ATAGI, 'ATAGI statement on revised recommendations on the use of COVID-19 Vaccine AstraZeneca, 17 June 2021' *ATAGI*, 17 June 2021, accessed 11 August 2022.
[8] B Lopez et al., 'Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant', *NEJM*, 2021, Vol. 385, pp. 585-94.
[9] S Nasreen et al., 'Effectiveness of COVID-19 vaccines against variants of concern in Ontario, Canada', *medRxiv*, preprint, 2021

percent, and by one dose of Spikevax (Moderna) is 80 percent.[10] Due to the very low rate of serious side effects and very high efficacy of the mRNA vaccines, ATAGI has recommended preferential use of these products over the Vaxzevria (AstraZeneca) vaccine.[11]

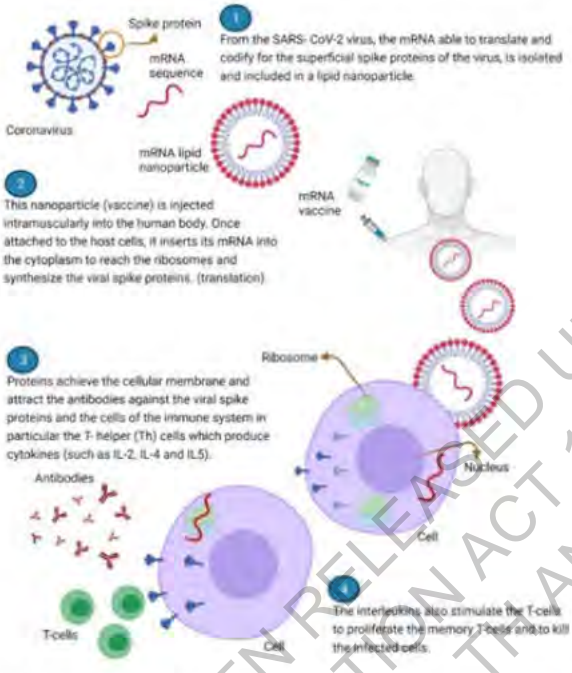


Figure 1: An overview of the mechanism of action of mRNA vaccines including Comirnaty (Pfizer) and Spikevax (Moderna), whereby the genetic code for the SARS-COV-2 spike protein enters cells from a fatty (lipid) capsule to induce production of the spike protein to simulate immune cells[12].

Myocarditis, inflammation of the heart or surrounding tissue, is a very rare side effect of the of Comirnaty (Pfizer) and Spikevax (Moderna) vaccines which is reported in 1-2 individuals per 100,000 injections.[13] The likelihood of myocarditis is significantly higher for boys aged 12-17 years of age (20 cases per 100,000 injections) and men aged under 30 (21 per 100,000 injections).[14] Due to the increased risk of myocarditis, ATAGI published clinical guidance recommending an increased dose interval for mRNA vaccines for those who are at greater risk of myocarditis or related cardiac side-effects[15]. Due to the slightly greater efficacy for preventing mild to moderate illness and rarity of potential side effects, ATAGI recommends a preference for mRNA vaccination over Vaxzevria (AstraZeneca) which was also available in Australia when this advice was first published.

[10] B Lopez et al., 'Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant', *NEJM*, 2021, Vol. 385, pp. 585-94 and S Nasreen et al., 'Effectiveness of COVID-19 vaccines against variants of concern in Ontario, Canada', *medRxiv*, preprint, 2021

[11] ATAGI, 'ATAGI statement on revised recommendations on the use of COVID-19 Vaccine AstraZeneca, 17 June 2021', *ATAGI*, 17 June 2021, accessed 11 August 2022.

[12] MT Mascellino et al., *'Overview of the Main Anti-SARS-CoV-2 Vaccines: Mechanism of Action, Efficacy and Safety', Infection and Drug Resistance*, 2021, Vol. 14, pp. 3459-3476.

[13] TGA, 'COVID-19 vaccine safety report - 28-07-2022', *TGA*, 28 July 2022, accessed 11 August 2022.

[14] TGA, 28 July 2022

[15] ATAGI, 'Guidance on Myocarditis and Pericarditis after mRNA COVID-19 Vaccines', *ATAGI,* 29 April 2022, accessed 11 August 2022.

Novavax

The Nuvaxovid (Novavax) protein-based vaccine contains pre-made copies of the SARS-CoV-2 spike protein which are injected via needle to elicit immune response.[16] Nuvaxovid (Novavax) was found to have 86.9 percent efficacy at preventing severe illness after two doses[17]. Myocarditis and other cardiac inflammation are potential side effects of Nuvaxovid (Novavax) injection, which have been reported in up to 24 individuals in Australia from a total of approximately 189,200 doses.[18]

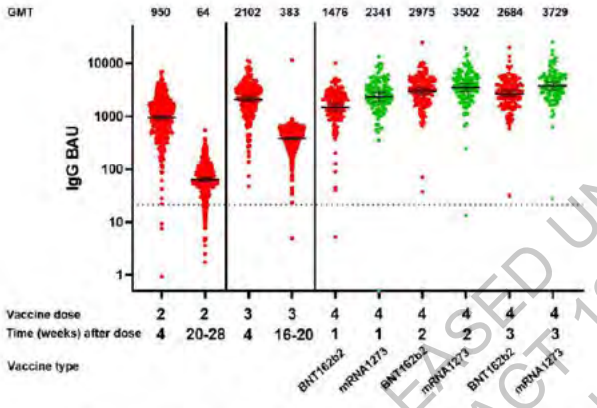


Figure 2: The immune response as measured in IgG BAU (Immunoglobulin binding antibody units) following second, third, and fourth doses of mRNA vaccine at various intervals following vaccination. Red measures are from individuals vaccinated with Comirnaty/BNT162b2 (Pfizer) and green measures are from individuals vaccinated with Spikevax/mRNA1273 (Moderna).[19]

The immune protection offered by vaccination with all types of vaccine has been shown to diminish over time and increase the chance of breakthrough infections even when fully vaccinated. However, studies show that immune protection can be increased above levels achieved from the primary 2 dose schedule with the administration of a third dose (booster dose) to individuals. [20] As such, ATAGI has recommended a booster dose of an eligible vaccine product for all Australians aged over 16 and certain individuals aged 12-15.[21] Further, ATAGI has recommended a fourth dose of an eligible vaccine product for all individuals aged over 30 years or those aged 16 years or older with a medical condition which increases the risk of severe COVID-19.[22] Studies have shown that a fourth dose is able to increase immune protection back to the same level achieved following a third dose.[23] Figure 2 shows the measured immune response of individuals diminishes in the weeks following a second or third dose of the Comirnarty/BNT162b2 (Pfizer) product but can be restored to peak levels following a fourth dose with either Comirnarty/BNT162b2 (Pfizer) or Spikevax/mRNA1273

[16] P Doherty, 'Issue #84: Viruses, Vaccines and COVID-19: arming up', *Doherty Institute*, 22 November 2021, accessed 11 August 2022.
[17] P Heath et al., 'Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine', *NEJM*, 2021, Vol. 385, pp. 1172-83.
[18] TGA, 'COVID-19 vaccine safety report - 28-07-2022', *TGA*, 28 July 2022, accessed 11 August 2022.
[19] G Regev-Yochay et al.
[20] K Gupta et al., 'COVID-19 vaccine breakthrough infections', *Science*, 2021, Vol. 374, pp. 1561-1562.
[21] ATAGI, 'Australian Technical Advisory Group on Immunisation (ATAGI) recommendations on the use of a booster dose of COVID-19 vaccine', *ATAGI,* 07 July 2022, accessed 11 August 2022.
[22] ATAGI, 'ATAGI updated recommendations for a winter dose of COVID-19 vaccine', *ATAGI,* 07 July 2022, accessed 09 August 2022.
[23] G Regev-Yochay et al., '4th Dose COVID mRNA Vaccines' Immunogenicity & Efficacy Against Omicron VOC', *medRxiv.* 15 February 15, 2022.

(Moderna).[24] Preliminary studies indicate that the high levels of protection achieved from a fourth dose may last for up to 30 days following vaccination; however, long term data on protection following a fourth dose is not yet available.[25]

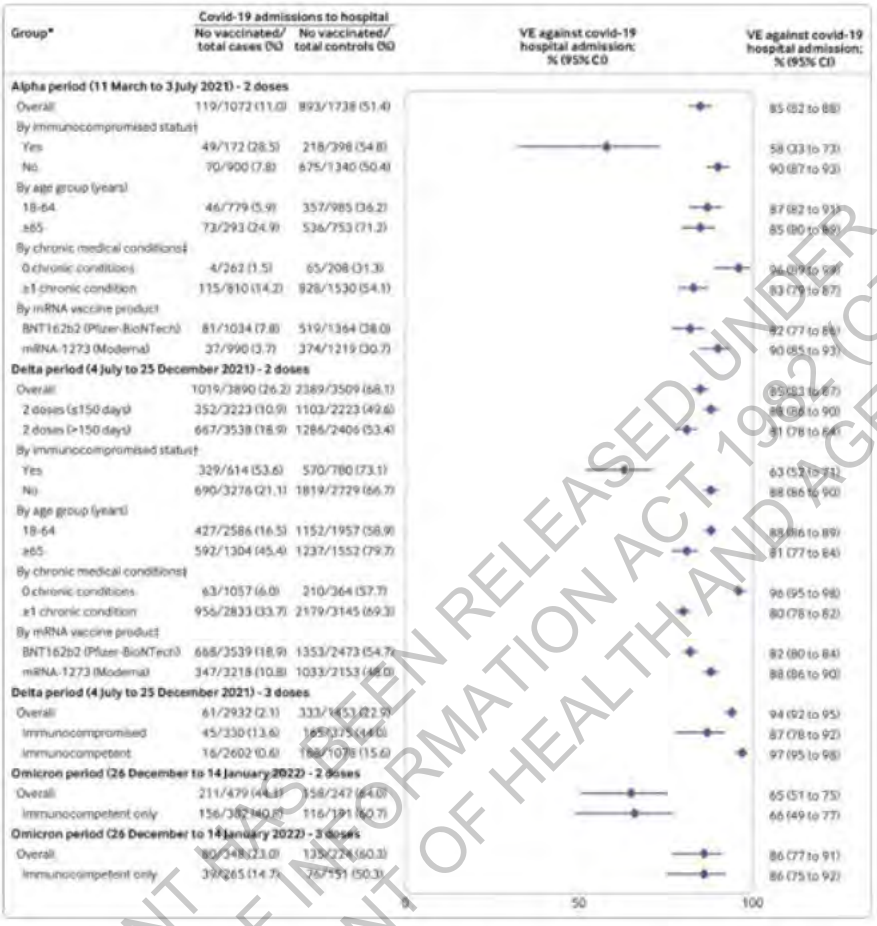


Figure 3: The Vaccine Efficacy (VE) of mRNA vaccines against hospital administration in the United States of America against the Alpha, Delta, and Omicron variants. Data on the Alpha and Delta waves includes detailed breakdowns on immunocompromised status, age, and type of mRNA vaccine used (Comirnaty/BNT162b2 (Pfizer) or Spikevax/mRNA1273 (Moderna)). Data on against all variants includes a breakdown on VE following 2 or 3 doses of mRNA vaccine.[26]

Despite immunity waning over time, vaccines which have been approved for use in Australia are safe and effective at reducing the risk of serious illness and deaths stemming from the original variant and subsequent variants of SARS-CoV-2. However, early studies indicate they likely have reduced efficacy against newer variants, especially in the prevention of mild illness.[27] The efficacy of two doses of an existing mRNA vaccine product against hospitalisation following infection with some SARS-CoV-2 variants, including the Alpha and Delta variants, is similar to the efficacy against the wild

[24] G Regev-Yochay et al., 2022
[25] O Magen et al., 'Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting', *NEJM*, 2022, Vol. 386, pp. 1603-1614.
[26] AS Lauring et al., 2022
[27] S Chalkias et al., 'A Bivalent Omicron-containing Booster Vaccine Against Covid-19', *medRxiv*. 25 June 2022.

type variant. However, three doses of mRNA vaccine are required to achieve the same level of protection against the Omicron variant.[28] In addition, the severity or progression of illness following hospitalisation is reduced for all variants following vaccination.[29] Overall, administration of a booster dose of any vaccine approved for use in Australia has been shown to increase the immune response to infection with the Omicron variant, highlighting the importance of vaccination to reduce the severity of infection in the current phase of the pandemic in Australia.[30]

Increased protection provided by a fourth dose against the Omicron variant is less significant than the protection against other variants for mild disease (see Figure 4). While these initial neutralization studies suggest increased protection, further studies of ongoing T cell responses are required to better understand the potential long-term protection against serious disease and deaths provided by a fourth dose.

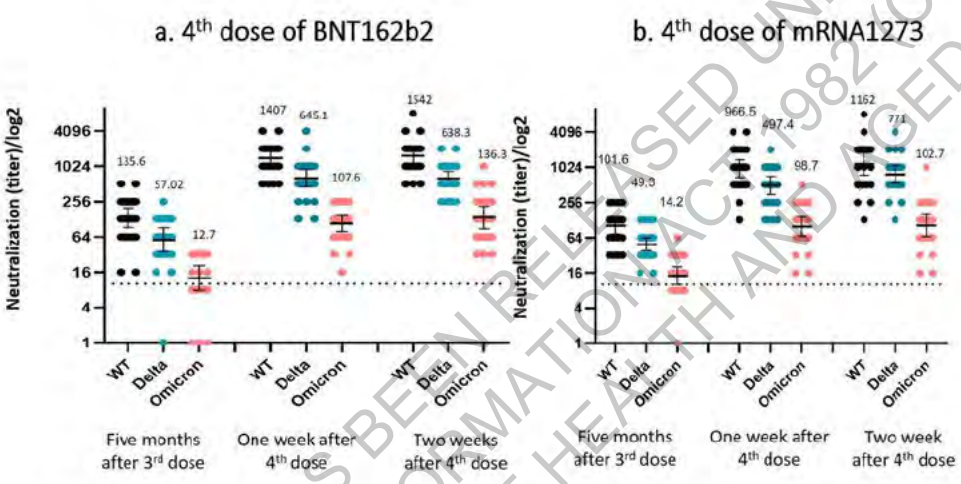


Figure 4: The live virus neutralisation efficacy of a. Comirnaty/BNT162b2 (Pfizer) and b. Spikevax/mRNA1273 (Moderna) against the wild type (WT), Delta, and Omicron variants of SARS-CoV-2 measured 5 months after a 3rd dose, one week after a 4th dose, and two weeks after a 4th dose.[31]

[28] AS Lauring et al., 'Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study', *BMJ*, 2022, Vol. 376.
[29] AS Lauring et al., 2022
[30] J Bowen et al., 'Omicron spike function and neutralizing activity elicited by a comprehensive panel of vaccines', *Science*, July 2022.
[31] G Regev-Yochay et al., '4th Dose COVID mRNA Vaccines' Immunogenicity & Efficacy Against Omicron VOC', *medRxiv*. 15 February 15, 2022.

Attachment 5: Treatments

Veklury® (remdesivir) by Gilead Sciences

Veklury was the first COVID-19 treatment provisionally approved by the TGA as a treatment option for COVID-19 to treat both severe COVID-19 and mild to moderate COVID-19. Veklury is a broad-spectrum antiviral medication administered as daily intravenous (IV) infusions. Treatment can take between three to ten days of daily intravenous infusion depending on the severity of symptoms. Veklury assists in the preventing the progression of COVID-19 symptoms by directly inhibiting the SARS-CoV-2 replication inside the infected cells through targeting the viral RNA polymerase (see Figure 1).

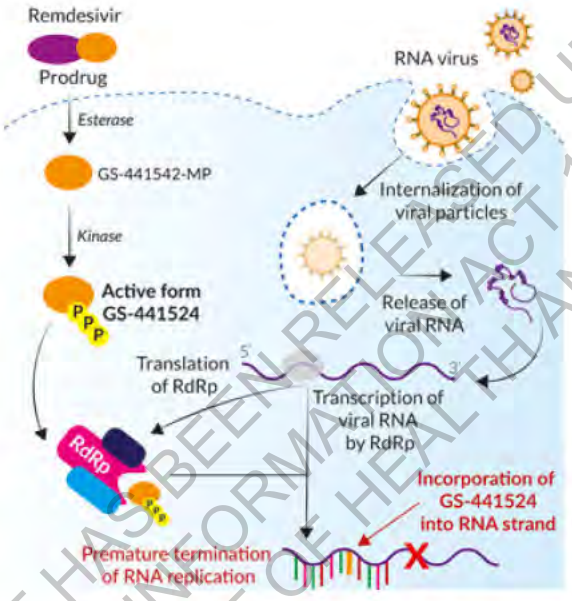


Figure 1: Remdesivir Mechanism of Action.[1]

Remdesivir inhibits the viral RNA-dependent RNA-polymerase (RdRp) enzyme, which is crucial for replication of the virus. Remdesivir is rapidly metabolised into a nucleoside monophosphate (GS-441542 MP) once it enters the cell. GS-441542 MP is processed further into GS-441524 which is an adenosine triphosphate (ATP) analogue and therefore can be used as a substrate by viral RdRp. GS-441524 competes with ATP to be incorporated into newly synthesised RNA strand. This leads to premature termination of the RNA replication process.

There is mixed clinical evidence available and limited data on the effectiveness of Veklury in the treatment of COVID-19. In May 2022, The Annals of Internal Medicine published a living systemic review and meta-analysis on Veklury use for adults with COVID-19.

This review collated results from five randomised-controlled trials (RCT) and two sub-trials completed from 1 January 2020 to 19 October 2021. Key findings reported were:

- Veklury use probably moderately increases the proportion of patients recovered by day 29;
- Veklury may reduce time to clinical improvement and reduce hospital length of stay; and

[1] InvivoGen, 'Remdesivir', *InvivoGen*, accessed 22 August 2022

- Veklury probably results in a small reduction in the proportion of patients receiving ventilation or extracorporeal membrane oxygenation (ECMO) at specific follow-up times. [2]

A retrospective comparative effectiveness study of 96,859 hospitalised COVID-19 patients was also conducted in the United States (between 23 February 2020 to 11 February 2021) to test real world effectives of Veklury. The study established that Veklury recipients who received at least one dose (n=42,473) were significantly more likely to achieve clinical improvement by day 28 but with an adjusted hazard ratio of only 1.19.[3]

Benefits were also reported by another small retrospective real-world effectiveness study of hospitalised COVID-19 patients treated with Veklury (n=163) versus other treatments (n=403) which showed that the Veklury treatment was associated with a 34 percent lower mortality rate.[4] Concurrent with these findings, a nationwide registry-based study in Italy of 16,462 people reported that treatment with Veklury within two days of hospital admission reduced the risk of death by approximately 40 percent.[5]

Gilead is actively recruiting for its Phase 2/3 CARAVAN clinical trial which seeks to evaluate the safety, tolerability, pharmacokinetics, and efficacy of Veklury in participants from birth to <18 years of age with COVID-19. This study is expected to be completed in February 2023.

Veklury is reported to retain neutralising activity against omicron subvariants BA.2.12.1, BA.4 and BA.5, with similar efficacy in comparison to the original SARS-CoV-2 ancestral strain based on in vitro pseudoviral assays.[6]

Utilisation

Veklury (remdesivir) is the most utilised IV treatment in Australia. Veklury is supplied through state and territory hospitals for the treatment of patients in hospital with moderate to severe symptomatic COVID-19 and for the prevention of severe COVID-19 in patients with mild to moderate symptoms. Since July 2020 almost 158,000 vials of Veklury have been administered, this equates to approximately 26,000 to 39,000 patients.

Veeklury is delivered with a minimum of 30 months shelf-life. It is the only treatment provided to the states and territories for the treatment of COVID-19 in patients in hospital with moderate to severe symptoms. Veklury is well utilised by the states and with the long shelf-life there should be adequate stocks available with minimal wastage.

Lagevrio® (Molnupiriavir) by Merck, Sharp and Dohme

Lagevrio is an oral antiviral treatment that inhibits viral replication of the SARS-CoV-2 virus. Lagevrio is a prescription-only, five-day course of oral capsules.

[2] A Kaka et al., 'Remdesivir for Adults With COVID-19: A Living Systematic Review and Meta-analysis for the American College of Physicians Practice Points', *Annuals of Internal Medicine*, 2022, 175:701-709.
[3] BT Garibaldi et.al., 'Real-World Effectiveness of Remdesivir In Adults Hospitalized With Covid-19: A Retrospective, Multicenter Comparative Effectiveness Study', *Clinical infectious Disease*, 2021. 15 December 2021.
[4] L Boglione et al., 'Remdesivir treatment in hospitalized patients affected by COVID-19 pneumonia: A case-control study', *J Med Virol,* 2022, Aug; 94(8): 3653–3660.
[5] P Russo et al., 'Mortality in SARS-CoV-2 Hospitalized Patients Treated with Remdesivir: A Nationwide, Registry-Based Study in Italy', *Viruses*, 2022, **14**(6), 1197.
[6] E Takashita et al., 'Efficacy of Antibodies and Antiviral Drugs against Omicron BA.2.12.1, BA.4, and BA.5 Subvariants', *New England Journal of Medicine*, 2022. **387**(5): p. 468-470.

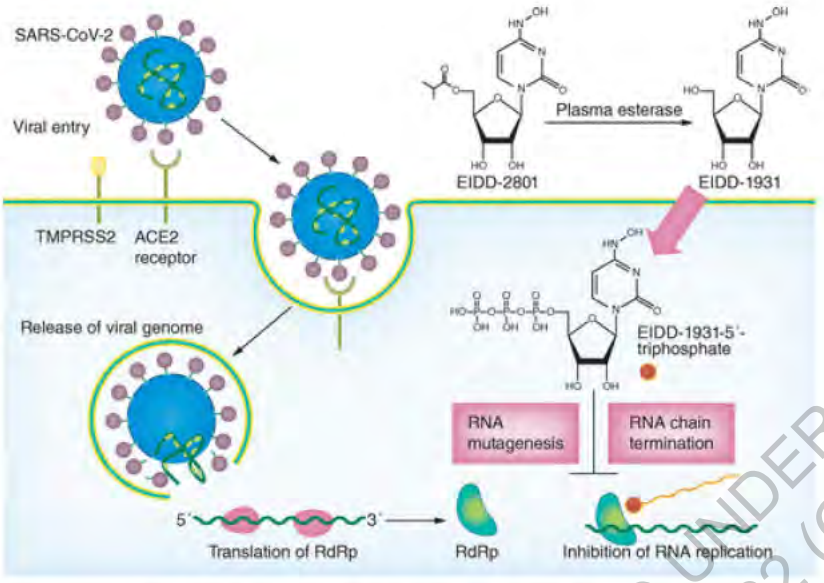


Figure 2: Molnupiravir Mechanism of action.[7]

Molnupiravir (EIDD-2801) is converted to its active form N4-hydroxycytidine (NHC; EIDD-1931) by an enzyme called, plasma esterase. Upon conversion, NHC is distributed in body tissues and fluid. In the body, a compound known as phosphate attaches itself to NHC to make NHC 5'-triphosphate (NT). This causes the RNA dependant RNA polymerase (RdRp) enzyme, which enables the SARS-CoV-2 virus make copies of itself, to incorrectly use NT in place of uridine triphosphate and cytidine triphosphate which are components that are required for viral replication. Once NT is incorporated into the RNA it introduces detrimental mutations preventing replication of the virus.

Lagevrio has been found to be effective in real world data. An observational retrospective cohort study of hospitalised patients (n=40,776) conducted in Hong Kong, between 26 February 2022 and 26 April 2022 (predominantly BA.2 variant), indicated that Lagevrio significantly lowered risk of disease progression, with the study reporting a hazard ratio of 0.53. Similar results were also seen for all-cause mortality, with the hazard ratio standing at 0.55 for Lagevrio.[8]

The UK National Health System has funded the Panoramic trial to study the community-based treatment of COVID-19 using antiviral treatments, Lagevrio and Paxlovid. The Lagevrio arm of the study was launched in December 2021. The study has recruited over 26,000 participants, making it the largest study of community-based treatments for acute COVID-19. Results from the trial are imminent.[9]

MSD is currently recruiting for the MOVe-Ahead phase 3 clinical trial to assess if Lagevrio will prevent symptomatic COVID-19 in adults who live with someone with confirmed COVID-19 infection (post exposure prophylaxis).

The MOVe-OUT trial (Phase 3, placebo controlled) evaluated the efficacy and safety of treatment with 800 mg of Lagevrio (twice daily for 5 days) started within 5 days after the onset of signs or

[7] S Khiali et al., 'Comprehensive review on molnupiravir in COVID-19: a novel promising antiviral to combat the pandemic', *Future Medicine*, 24 February 2022, accessed 28 August 2022.
[8] CKH Wong et al., 'Real-world effectiveness of molnupiravir and nirmatrelvir/ritonavir among COVID-19 inpatients during Hong Kong's Omicron BA.2 wave: an observational study', *medRxiv*, 2022, 19 May 2022.
[9] University of Oxford, 'New antiviral, Paxlovid, added to PANORAMIC study', *Nuffield Department of Primary Care Health Services,* 12 April 2022, accessed 22 August 2022.

symptoms in non-hospitalised, unvaccinated adults with mild-to-moderate, laboratory-confirmed COVID-19 and at least one risk factor for severe COVID-19 illness.

The interim analysis showed an efficacy of approximately 50 percent with respect to the primary outcome of hospitalisation for any cause or death through day 29, with a primary outcome event occurring in 28 of 385 participants who received Lagevrio and in 53 of 377 participants who received placebo. The final results published indicated that the efficacy later decreased to approximately 30 per cent (a primary outcome event occurred in 48 of 709 participants who received Lagevrio and in 68 of 699 participants who received placebo).[10]

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MSD is currently recruiting for the MOVe-Ahead phase 3 clinical trial sees to assess if Lagevrio will prevent symptomatic COVID-19 in adults who live with someone with confirmed COVID-19 infection (post exposure prophylaxis).

Utilisation

With the combination of the expansion of the PBS criteria on 11 July 2022 and the increase in COVID-19 cases associated with the Omicron BA.4 and BA.5 wave in Australia, uptake of the oral treatments through the PBS saw a significant increase, which peak in the week of 18 July 2022. Prescription levels of the antivirals has steadily decreased since following the downward trend of COVID-19 case numbers in Australia.

Since listing to 21 August 2022, over 245,550 PBS subsidised prescriptions for COVID-19 oral treatments have been dispensed, approximately 196,890 courses for Lagevrio (molnupiravir). This compares to around 29,300 courses through NMS channels. The uptake of Lagevrio to date is approximately 3.4 times higher than the uptake of Paxlovid, likely related to Lagevrio's much lower potential for interactions with other commonly used prescription drugs and that older people are commonly using.

The TGA has approved an extension to the shelf-life Lagevrio to 18 months. s47C, s34(3)

[redacted]

[10] A Jayk Bernal et al., 'Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients', *New England Journal of Medicine*, 2021. 386(6): p. 509-520.
[11] CKH Wong et al., 'Real-world effectiveness of molnupiravir and nirmatrelvir/ritonavir among COVID-19 inpatients during Hong Kong's Omicron BA.2 wave: an observational study', *medRxiv*, 2022, 19 May 2022.
[12] University of Oxford, 'New antiviral, Paxlovid, added to PANORAMIC study', *Nuffield Department of Primary Care Health Services,* 12 April 2022, accessed 22 August 2022.

Paxlovid® (nirmatrelvir and ritonavir) by Pfizer

Paxlovid (nirmatrelvir and ritonavir) is an oral antiviral combination therapy, the nirmatrelvir component blocks the activity of a protease enzyme that the coronavirus needs to replicate. Nirmatrelvir (150mg) is administered once a day for five days in combination with low-dose ritonavir (150) to maintain plasma levels of nirmatrelvir for the duration of the treatment.

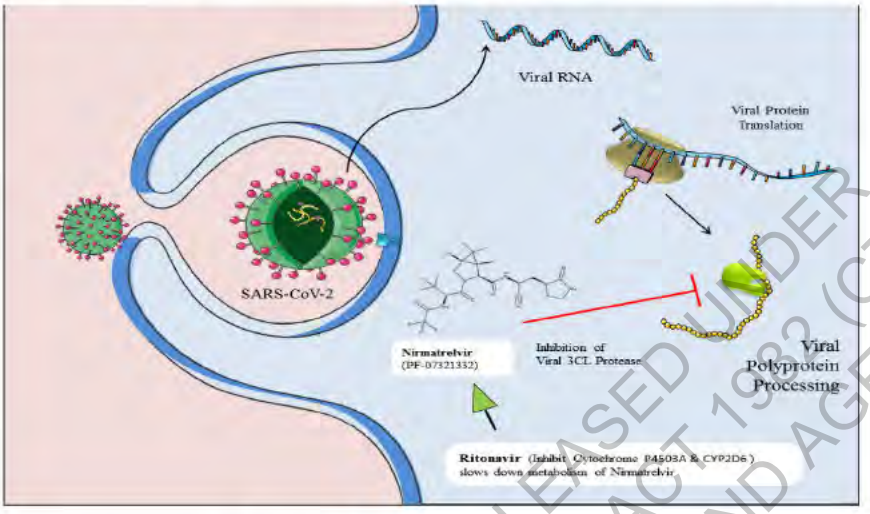

Figure 3: Paxlovid mechanism of action.[13]

Paxlovid is a combination of two drugs, namely, nirmatrelvir and ritonavir. Nirmatrelvir is an orally bioavailable peptidomimetic inhibitor of the 3C-like protease (3CLPRO) enzyme. 3CLPRO is involved in cleaving polyproteins 1a and 1ab of the SARS-CoV-2 virus. Without the function of the SARS-CoV-2 3CLPRO enzyme, non-structural proteins such as proteases are unable to fulfill their functions, thereby inhibiting viral replication. Ritonavir slows down the metabolism of nirmatrelvir mediated by CYP3A and increases the plasma concertation of nirmatrelivir.

Paxlovid was granted provisional approval by the TGA on 18 January 2022 for the treatment of COVID-19 in adults 18 years of age and older, who do not require initiation of supplemental oxygen due to COVID-19 and are at increased risk of progression to hospitalisation or death.[14]

Paxlovid has shown efficacy in both clinical trials and real-world studies. The EPIC-HR trial (phase II/III randomised controlled trial) focused on symptomatic, unvaccinated, non-hospitalised adults (n=2246) patients at high risk for progression to severe COVID-19. Patients were assigned in a 1:1 ratio to receive either 300mg of nirmatrelvir plus 100 mg of ritonavir (or placebo every 12 hours for 5 days). The final results were consistent with the interim analysis announced in November 2021 showing Paxlovid significantly reduced the risk of hospitalisation, or death for any cause by 89 percent, compared to placebo in non-hospitalised, high-risk adult patients with COVID-19 treated within three days of symptom onset.[15]

[13] A Vitiello et al. '[Pandemic COVID-19, an update of current status and new therapeutic strategies]', *Naunyn-Schmiedeberg's Arch Pharmacol*, 02 July 2022, accessed 21 August 2022

[14] TGA, '[TGA provisionally approves Pfizer Australia Pty Ltd's COVID-19 treatment nirmatrelvir + ritonavir (PAXLOVID)]', *TGA*, 02 August 2022, accessed 21 August 2022.

[15] J Hammond et al., 'Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19', *New England Journal of Medicine*, 2022. 386(15): p. 1397-1408.

The EPIC-SR clinical trial (n=1,100) sought to determine the effectiveness of Paxlovid in a broader population, including "standard-risk" vaccinated adults. Findings in this relatively small study, showed that Paxlovid reduced the relative risk of hospitalisation or death versus placebo by 51 percent, but the difference between groups was not statistically significant. Among vaccinated adults with at least one risk factor for severe COVID-19, Paxlovid lowered the risk of hospitalisation or death by 57 percent, however, the effect was not statistically significant. Therefore, Pfizer plans to halt further enrolment into this study.[16]

Paxlovid has also shown to be effective in real world studies. An observational retrospective cohort study of hospitalised patients (n=40,776) conducted in Hong Kong, between 26 February 2022 and 26 April 2022 (predominantly BA.2 variant), indicated that Paxlovid significantly lowered risk of disease progression, with the study reporting a hazard ratio of 0.33. Similar results were also seen for all-cause mortality, with the hazard ratio standing at 0.32 for Paxlovid.[17]

Another similar cohort study from Israel, conducted between 9 January 2022 to 10 March 2022 (predominantly B.1.1.529 variant), concluded that Paxlovid is most effective in vulnerable people aged 65 and older. Paxlovid treatment was associated with a 67 percent reduction in COVID19 hospitalisations and an 81 percent reduction in COVID-19 mortality in patients 65 years and above. While the study found Paxlovid to be effective in older populations, the study also found that Paxlovid had 'no significant impact' on a younger cohort aged 40–64.[18]

On 12 April 2022, a Paxlovid arm was added into the UK adaptive platform Panoramic study to investigate the real-world effectiveness of COVID-19 treatments in reducing recovery time and hospitalisation. The trial of Paxlovid is still recruiting.[19]

Pfizer is undertaking additional clinical trials on the use pf Paxlovid. On 9 March 2022, Pfizer initiated a Phase 2/3 study, EPIC-PEDS clinical trial to evaluate the safety, pharmacokinetics, and efficacy of Paxlovid in non-hospitalised, symptomatic, paediatric participants (under 18) with a confirmed diagnosis of COVID-19 who are at risk of progression to severe disease. The study is still recruiting.[20] On 28 March 2022, Pfizer also reported that Paxlovid will be investigated in the RECOVERY trial as a potential treatment for patients hospitalised with COVID-19. The trial is still recruiting.[21]

Utilisation

With the combination of the expansion of the PBS criteria on 11 July 2022 and the increase in COVID-19 cases associated with the Omicron BA.4 and BA.5 wave in Australia, uptake of the oral treatments through the PBS saw a significant increase, which peaked in the week of 18 July 2022. Prescription levels of the antivirals has steadily decreased since following the downward trend of COVID-19 case numbers in Australia.

[16] N Pagliarulo, 'Pfizer study results show Paxlovid benefit less clear in lower-risk patients', *Healthcare Dive,* 16 June 2022, accessed 16 August 2022.
[17] CKH Wong et al., 'Real-world effectiveness of molnupiravir and nirmatrelvir/ritonavir among COVID-19 inpatients during Hong Kong's Omicron BA.2 wave: an observational study', *medRxiv*, 2022, 19 May 2022.
[18] Y Ronen Arbel, 'Oral Nirmatrelvir and Severe Covid-19 Outcomes During the Omicron Surge', *Research Square*, 2022.
[19] University of Oxford, 'New antiviral, Paxlovid, added to PANORAMIC study', *Nuffield Department of Primary Care Health Services,* 12 April 2022, accessed 22 August 2022.
[20] Pfizer Pty Ltd, 'Pfizer Initiates Phase 2/3 Study of Novel COVID-19 Oral Treatment in Pediatric Participants', *Pfizer Pty Ltd,* 09 March 2022, accessed 22 August 2022.
[21] University of Oxford, 'Paxlovid to be investigated by the RECOVERY Trial as a potential treatment for patients hospitalised with COVID-19', 28 March 2022, accessed 16 August 2022.

Since listing to 21 August 2022, over 245,550 PBS subsidised prescriptions for COVID-19 oral treatments have been dispensed, including approximately 48,660 courses for Paxlovid (nirmatrelvir & ritonavir). This compares to around 22,200 courses prescribed through NMS channels.

The uptake of Lagevrio to date is approximately 3.4 times higher than the uptake of Paxlovid. This is despite the available clinical evidence suggesting Paxlovid is more effective than Lagevrio in preventing hospitalisations and death, noting- the clinical trial data was generated prior to the Omicron waves and no head-to-head comparisons are available.

s47C, s34(3)

As Lagevrio was listed on the PBS two months before Paxlovid, more prescribers may have experience prescribing Lagevrio.

In July 2022, the TGA approved an extension to the shelf-life of Paxlovid to 18 months, this will extend stock remaining until May 2023. s47C, s34(3)

s45, s47C, s47E, s34(3)

Evusheld® (tixagevimab and cilgavimab) by AstraZenca

Evusheld is comprised of two monoclonal antibodies, namely, tixagevimab and cilgavimab. These antibodies bind to the spike protein of the SARS-CoV-2 virus at two different sites to stop the virus from entering the body's cells and causing infection. In Australia, Evusheld is currently administered as two separate, sequential injections of two the long-acting monoclonal antibodies, tixagevimab (150mg) and cilgavimab (150mg).

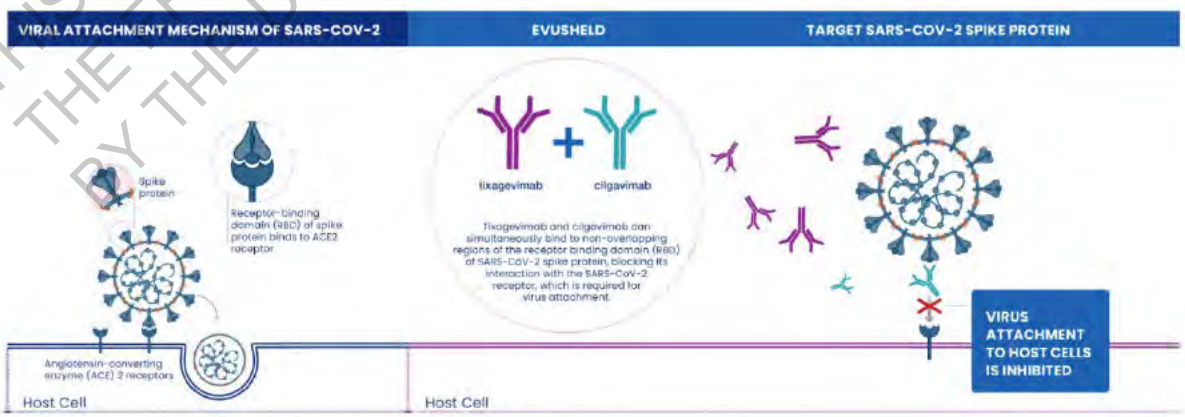

Figure 4: Evusheld mechanism of action.[22]
Evusheld is the combination of two monoclonal antibodies, namely, Tixagevimab and Cligavimab. Both antibodies bind to non-overlapping regions of the receptor binding domain (RBD) of SARS-CoV-2 spike protein, blocking its interaction with the SARS-CoV-2 receptor, which is required for virus attachment.

The primary source of evidence for Evusheld for PrEP is a head-to-head trial comparing a single dose of Evusheld 150-150mg to placebo (PROVENT).[23] s47, 47E, s34(3) The study recruited 5197 participants who were randomized (3460 active group, 1737 placebo group). The primary analysis was conducted after a median follow up if 83 days. Symptomatic COVID-19 occurred in 0.2 percent in the Evusheld group and 1.0 percent in the placebo group (relative risk reduction 76.7 percent). Follow-up at median of 6 months showed a relative risk reduction of 83 percent. Five cases of severe or critical COVID-19 and two COVID-19-related deaths occurred, all in the placebo group.

At the follow up at median of 6 months, a higher proportion of subjects who received Evusheld versus placebo reported myocardial infarction and cardiac failure serious adverse events (SAE). All subjects who experienced cardiac SAE had cardiac risk factors and/or a prior history of cardiovascular disease at baseline. At the same follow up, a higher incidence of thromboembolic SAE was reported in subjects who received Evusheld, compared to placebo.[25]

On 14 July 2022, AstraZeneca revised the recommended dosage for Evusheld for PrEP of COVID-19. The AstraZeneca statement advises the updated recommended dosage regimen is 300 mg tixagevimab and 300 mg cilgavimab every six months (i.e., a four -fold dose increase). The statement says the "update is based on the latest information available, including new safety and efficacy data from the ongoing PROVENT Phase III trial, emerging real-world evidence in immunocompromised patients who received 600 mg during Omicron and modelling assessments against BA.2, BA.4 and BA.5 based on neutralisation activity".[26]

Previously, on 24 February 2022, the US FDA revised the emergency use authorisation for Evusheld to double the dose to 300mg-300mg. On 29 June 2022, the FDA again revised the emergency use authorisation for PrEP to include repeat dosing every 6 months.[27] An application to increase the dose of Evusheld was made to TGA in late July 2022 and is under evaluation.[28]

s47, 47E, s34(3)

s47, 47E, s34(3)

[22] L Huynh, 'What Is Evusheld', *Prestons Pharmacy,* 03 January 2022, accessed 18 August 2022
[23] M Levin et al., 'Intramuscular AZD7442 (Tixagevimab–Cilgavimab) for Prevention of Covid-19', *New England Journal of Medicine,* 09 June 2022, accessed 18 August 2022
s47, 47E, s34(3)
[25] TGA, *Provisionally Approved Product Information Evusheld*, accessed 18 August 2022
[26] AstraZeneca, 'Update to Evusheld recommended dosage regimen for pre-exposure prophylaxis of COVID-19 [media release]', *AstraZeneca,* 14 July 2022, accessed 22 July 2022.
[27] FDA, 'FDA authorizes revisions to Evusheld dosing', 29 July 2022, accessed 21 August 2022.
[28] TGA, 'COVID-19 treatments: Treatments undergoing evaluation', 18 August 2022, accessed 28 August 2022.

s47, 47E, s34(3)

Patients given Evusheld had a lower incidence of the serious illness from SARS-CoV-2 infection, COVID-19-related hospitalisation, or mortality (HR 0.31; 95 percent CI, 0.18-0.53). The rates of adverse events were not reported. [29]

Another retrospective cohort study compared the efficacy of Evusheld in a sample of 222 solid organ transplant recipients who received Evusheld for PrEP and 222 vaccine-matched solid organ transplant recipients. At a mean follow-up of 87 ± 30 days after active treatment, 5 percent of subjects developed breakthrough SARS-CoV-2 infections, of whom one required hospitalisation and none died. In the control group, 14 percent of subjects developed SARS-CoV-2 infections, of whom six were hospitalised and three died at a mean follow-up of 82 ± 28 days. In the active treatment group, the incidence rate of breakthrough SARS-CoV-2 infection was higher in those who received the lower (150–150 mg) dose compared to those who received the higher dose of 300–300 mg (log-rank p = 0.025). There is no indication patients were re-dosed. [30]

Utilisation

A total of 36,000 doses of Evusheld were procured and stocks were deployed to the states and territories. s47, 47C, s34(3)

s47, 47C, s34(3)

Xevudy® (sotrovimab) by GlaxoSmithKline

Xevudy is a monoclonal antibody treatment which works by binding to the SARS-CoV-2 spike protein. This blocks the virus entering human cells and multiplying in the body. Xevudy (500mg) is administered by a single intravenous infusion within five days of symptom onset.

[29] Y Young-Xu et al., 'Tixagevimab/Cilgavimab for Prevention of COVID-19 during the Omicron Surge: Retrospective Analysis of National VA Electronic Data', *medRxiv*, 2022: p. 2022.05.28.22275716.
[30] A Al Jurdi et al., 'Tixagevimab/cilgavimab pre-exposure prophylaxis is associated with lower breakthrough infection risk in vaccinated solid organ transplant recipients during the omicron wave', *American Journal of Transplantation*, 2022, ajt.17128.

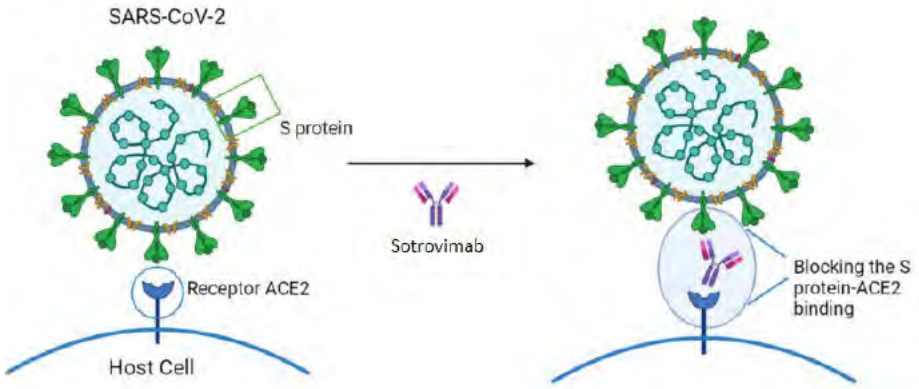

Figure 5: Sotrovimab Mechanism of Action.[31]
Sotrovimab is a monoclonal antibody that binds with high affinity to a conserved region on the receptor binding domain of the spike protein of SARS-CoV-2 virus and disrupts binding of the virus to ACE2 on the host cell, preventing attachment.

In late 2021 clinical trial evidence and observational data from Australia and internationally demonstrated Xevudy as a well-tolerated and highly effective treatment preventing severe disease and death in high-risk individuals.

On 8 November 2021, the Phase 3 placebo-controlled COMET-ICE trial evaluated the efficacy and safety of a single 500mg intravenous (IV) infusion of Xevudy in preventing progression of mild to moderate COVID-19 to severe disease in adults who were not hospitalised and not requiring oxygen. The primary efficacy analysis of all 1,057 patients in the COMET-ICE trial demonstrated a 79 percent reduction in hospitalisation for more than 24 hours, or death due to any cause by day 29, compared to placebo.[32] This meets the primary endpoint of the trial. Xevudy was also well tolerated, and no safety concerns were identified.

In addition, a real word large population cohort study in the United Arab Emirates found that Xevudy reduced the risk of progression of COVID-19 when administrated early to non-hospitalised patients with symptomatic COVID-19.[33] It lowered the risk of COVID-19 related hospitalisation or death. The most common variants observed during the study period were limited to the Alpha (11.3 percent), Beta (39.2 percent) and Delta (33.9 percent).

Despite high effectiveness against the earlier strains of COVID-19 such as Alpha, Delta and the Omicron BA.1 strains, several *in vitro* studies have reported that Xevudy lost neutralising activity against Omicron BA.2, BA2.75, BA.4 and BA.5 in comparison to BA.1 and the ancestral strain.[34] [35]

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[31] A Torrente-López et al., 'The Relevance of Monoclonal Antibodies in the Treatment of COVID-19', *Vaccines,* 26 May 2021, accessed 20 August 2022
[32] A Gupta et al., 'Effect of the Neutralizing SARS-CoV-2 Antibody Sotrovimab in Preventing Progression of COVID19: A Randomized Clinical Trial', *medRxiv*, 2021: p. 2021.11.03.21265533.
[33] F Saheb Sharif-Askari et al., 'Sotrovimab Lowers the Risk of COVID-19 Related Hospitalization or Death in a Large Population Cohort in the United Arab Emirates', *Clinical Pharmacology & Therapeutics*. n/a
[34] E Takashita et al., 'Efficacy of Antibodies and Antiviral Drugs against Omicron BA.2.12.1, BA.4, and BA.5 Subvariants', *New England Journal of Medicine*, 2022. 387(5): p. 468-470.
[35] DJ Sheward et al., 'Evasion of neutralizing antibodies by Omicron sublineage BA.2.75', *bioRxiv*, 2022: p.2022.07.19.500716.

Advice was provided at the time to prescribers to only use Xevudy in confirmed Delta or Omicron BA.1 patients.

On 7 April 2022, the TGA received an application from GSK for a double dose (1000mg) of Xevudy. The TGA is waiting on further data from the sponsor to support the efficacy of the higher (1000 mg) dose of XEVUDY against the Omicron BA.2 sub-lineage.[36]

Prior to the loss of efficacy, Xevudy was a well utilised treatment for patients with mild to moderate symptoms through state and territory out-patient clinics. However, due to the loss in efficacy against recent Omicrons variants, there has been a significant decrease in the utilisation of Xevudy. s47C, s34(3)

Ronapreve® (casirivimab and imdevimab) by Roche

Ronapreve is a combination antibody treatment comprised of casirivimab and imdevimab. The two monoclonal antibodies bind to two different sites of the SARS-CoV-2 spike protein and flag the virus as 'foreign', prompting the body's immune response.

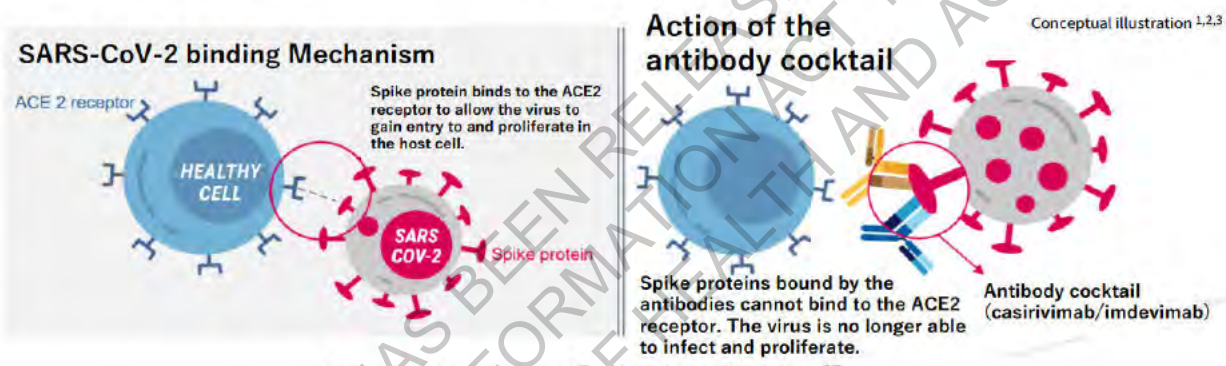


Figure 6: Ronapreve Mechanism of action.[37]

Ronapreve is a combination of two monoclonal antibodies casirivimab and imdevimab. Both antibodies bind non-competitively non overlapping regions of the spike protein and prevent viral replication by inhibiting viral entry into the host cell.

Similar to Xevudy, clinical evidence released in 2021 demonstrated high effectiveness of Ronapreve in both the treatment of mild to moderate COVID to prevent severe disease and death in high-risk individuals and also as a post-exposure prophylaxis in high-risk close contacts.

Results of the phase II/III REGN-COV 2066 study in non-hospitalised patients with COVID-19 at high risk of severe disease demonstrated that Ronapreve resolved symptoms and reduced the viral load within seven days compared to placebo. Ronapreve also reduced the relative risk of COVID-19 related hospitalisation or death by approximately 70 percent. Among patients who were hospitalised due to COVID-19, those who received Ronapreve had shorter hospital stays and a lower incidence of admission to an ICU than those in the placebo group.[38]

[36] TGA, 'Product information update for COVID-19 treatment, XEVUDY (sotrovimab)', *TGA*, 06 May 2022, accessed 20 August 2022.
[37] Roche, 'Striving to Develop Therapeutic Drugs for COVID-19', 30 August 2021, accessed 22 August 2022.
[38] DM Weinreich et al., 'REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19', *New England Journal of Medicine*, 2021. 385(23): p. e81.

A two part, randomised, double-blind, placebo-controlled trial conducted in the US, Romania and Moldova assessed the efficacy and safety of subcutaneous REGEN-COV in preventing SARS-CoV-2 infection among previously uninfected household contacts of infected persons (Part A) and in treating recently infected asymptomatic persons (Part B). Part A of the study reported that Ronapreve prevented symptomatic and asymptomatic COVID-19 infection in previously uninfected household contacts of infected persons. Among the participants who became infected, Ronapreve reduced the duration of symptomatic disease and the duration of a high viral load.[39]

Part B of the study determined that Ronapreve treatment significantly reduced the incidence of symptomatic COVID-19 (risk reduction = 13 percent) among recently exposed, asymptomatic individuals in comparison to placebo.[40]

Several real-world effectiveness studies have reported that Ronapreve was associated with a significantly lower rate of hospitalisation and reduced risk of mortality in patients infected with susceptible variants in comparison to the control arms.[41]

Despite ability to neutralise earlier strains of COVID-19 such as alpha and delta strains, Ronapreve has lost neutralising activity against the omicron subvariant BA.4 and BA.5 when compared to the BA.1 strain.[42] Ronapreve was also unable to neutralise the BA.1 strain of omicron in comparison to the delta strain.[43] Advice was provided to prescribers at the time to only use Ronapreve in confirmed Delta patients.

Due to the emerging SARS-CoV-2 variants impacting susceptibility to Ronapreve, there are no new clinical trials investigating the use of Ronapreve for other indications than those already approved by the TGA.

Due to the loss of efficacy against Omicrons variants, there has been a significant decrease in the utilisation of Ronapreve. s47C, s34(3)

Actemra® (tocilizumab) by Roche

Actemra is an immunosuppressive humanised monoclonal antibody used for the treatment of rheumatoid arthritis and systemic juvenile idiopathic arthritis, which was repurposed for the treatment of COVID-19.[44] Unlike other COVID-19 treatments, Actemra does not directly target SARS-CoV-2 proteins. Instead, it reduces inflammation by blocking the interleukin-6 receptor (IL-6),

[39] MP O'Brien et al., 'Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19', *New England Journal of Medicine*, 2021, 385(13): p. 1184-1195.
[40] MP O'Brien et al., 'Effect of Subcutaneous Casirivimab and Imdevimab Antibody Combination vs Placebo on Development of Symptomatic COVID-19 in Early Asymptomatic SARS-CoV-2 Infection: A Randomized Clinical Trial', *JAMA*, 2022. **327**(5): p. 432-441.
[41] PW Horby et al., 'Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial', *medRxiv*, 2021: p. 2021.06.15.21258542. and W Wei et al., 'Real-world Effectiveness of Casirivimab and Imdevimab in Patients With COVID-19 in the Ambulatory Setting: An Analysis of Two Large US National Claims Databases', *medRxiv*, 2022: p. 2022.02.28.22270796 and R Razonable et al., 'Casirivimab–Imdevimab treatment is associated with reduced rates of hospitalization among high-risk patients with mild to moderate coronavirus disease-19', *eClinicalMedicine*, 2021 and B Webb et al., 'Real-world Effectiveness and Tolerability of Monoclonal Antibody Therapy for Ambulatory Patients With Early COVID-19', *Open Forum Infectious Diseases*, 2021. 8(7).
[42] D Yamasoba et al., 'Neutralisation sensitivity of SARS-CoV-2 omicron subvariants to therapeutic monoclonal antibodies', *Lancet Infect Dis*, 2022. 22(7): p. 942-943.
[43] T Bruel et al., 'Serum neutralization of SARS-CoV-2 Omicron sublineages BA.1 and BA.2 in patients receiving monoclonal antibodies', *Nature Medicine*, 2022. 28(6): p. 1297-1302
[44] H Samaee, et al., 'Tocilizumab for treatment patients with COVID-19: Recommended medication for novel disease', *Int Immunopharmacol*, 2020. **89**(Pt A): p. 107018.

thereby helping to slow the effects of the virus by preventing IL-6 mediated signal transduction in the body and reduces the chance of a cytokine storm which increases the severity of illness.[45]

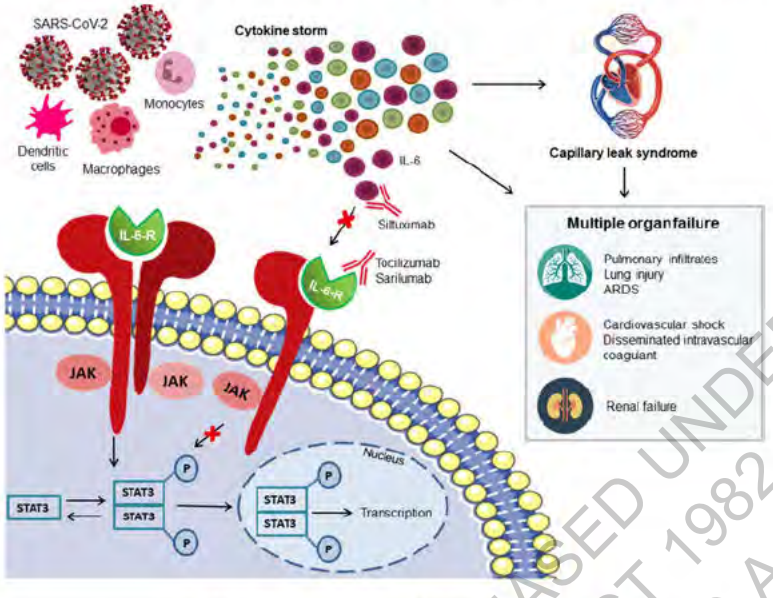


Figure 7: Actemra Mechanism of Action [46]

IL-6 pathway and Tocilizumab (TCZ) mechanism of action. Upon SARS-CoV-2 infection, immune cells such as macrophages release cytokines including IL-6. IL-6 binds to either the IL-6R cell receptor or soluble receptor (SIL-6R) which activates both the NF-κB and JAK/STAT cell signalling pathways which can lead to a cytokine storm. TCZ antibodies bind to the IL-6R and SIL-6R receptors to prevent this process and reduce the chance of cytokine storm.

Numerous clinical trials have investigated the potential of tocilizumab as a COVID-19 treatment. A key platform trial called RECOVERY evaluated the effects of tocilizumab in hospitalised COVID positive adult patients (n=4166) with both hypoxia and systemic inflammation. The authors reported that tocilizumab improved survival and other clinical outcomes.[47] Overall, 31 percent of patients allocated to tocilizumab and 35 percent of patients allocated to standard care died within 28 days. Patients allocated to tocilizumab were also more likely to be discharged from hospital within 28 days (57 percent vs 50 percent).

Several clinical trials continue to evaluate the use of the tocilizumab as a COVID-19 treatment. For example, the university of Chicago is evaluating a lower dose of tocilizumab in hospitalised COVID-19 patients (COVIDOSE-2).[48] Roche is also investigating the use of tocilizumab in paediatric patients hospitalised with COVID-19.[49] Both trials are currently in the recruitment stage.

[45] AG Kaye and R. Siegel, 'The efficacy of IL-6 inhibitor Tocilizumab in reducing severe COVID-19 mortality: a systematic review', *PeerJ*, 2020. 8: p. e10322.
[46] S Crisafulli, 'Potential Role of Anti-interleukin (IL)-6 Drugs in the Treatment of COVID-19: Rationale, Clinical Evidence and Risks', *BioDrugs,* 2020, 34, pg 415-422,
[47] O Abani et al., 'Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial', *The Lancet*, 2021. **397**(10285): p. 1637-1645.
[48] University of Chicago, 'Low-dose Tocilizumab Versus Standard of Care in Hospitalized Patients With COVID-19 (COVIDOSE-2)', *ClinicalTrials.gov,* 18 May 2022, accessed 18 August 2022.
[49] Hoffmann-La Roche, 'A Study Evaluating Tocilizumab in Pediatric Patients Hospitalized With COVID-19', 20 December 2021, 18 August 2022.

Antiviral Agents vs. Monoclonal Antibodies Treatments

Monoclonal Antibodies

Monoclonal antibodies (mAbs) are a type of immune system protein generated in the laboratory that can bind with high affinity to a certain target, such as a particular antigen on the surface of cells.[50]

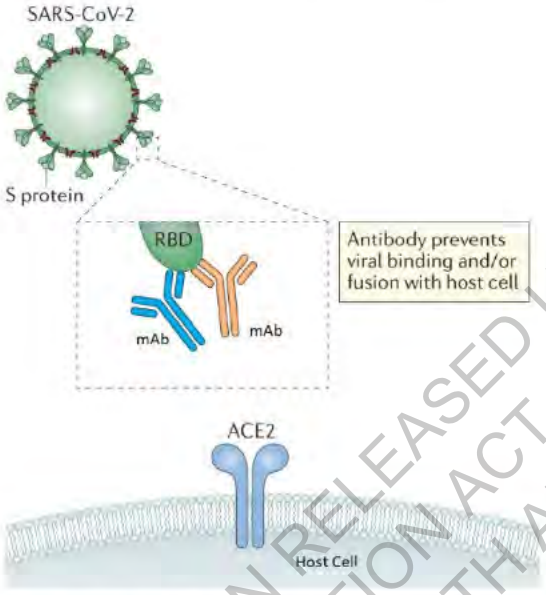


Figure 8: Inhibition of host cell engagement by neutralising monoclonal antibodies.[51]

In the case of COVID-19, the majority of monoclonal antibodies target the receptor binding domain (RBD) of the surface spike glycoprotein expressed on the SARS-CoV-2 virus. The spike protein enables viral entry into host cells through binding and fusion upon engaging the angiotensin-converting enzyme 2 (ACE2) receptor.[52] As depicted in Figure 8 above, monoclonal antibodies bind to the RBD of the spike protein and prevent the virus fusing with the host cell through the ACE2 receptor.[53]

Monoclonal antibodies can be used not just for the treatment of COVID-19, but also potentially for preexposure or post exposure prophylaxis (prevention) and may be beneficial to limit transmission in localised epidemics or small outbreaks such as in an aged care facility.[54] However, their benefits are impeded by mutations on the spike protein in emerging omicron variants that reduce the ability of the monoclonal antibody to recognise and bind to SARS-CoV-2.

Often, the target epitope (site) on the spike protein, for the monoclonal antibody to bind to, is chosen in the most conserved regions of the RBD. This deters the emergence of resistant SARS-CoV-2 strains that may be caused by continued use of monoclonal antibody treatment.[55]As an additional precautionary measure, some monoclonal treatment options use a

[50] A Aleem and A.K. Slenker, 'Monoclonal Antibody Therapy For High-Risk Coronavirus (COVID 19) Patients With Mild To Moderate Disease Presentations', *StatPearls*, 2022: Treasure Island (FL).
[51] P Taylor et al., 'Neutralizing monoclonal antibodies for treatment of COVID-19', *Nature Reviews Immunology*, 2021 pg 382 – 393
[52] M Marovich et al, 'Monoclonal Antibodies for Prevention and Treatment of COVID-19', *JAMA*, 2020. **324**(2): p. 131-132.
[53] PC Taylor et al., 'Neutralizing monoclonal antibodies for treatment of COVID-19', *Nature Reviews Immunology*, 2021, **21**(6): p. 382-393.
[54] D Focosi et al., 'Monoclonal antibody therapies against SARS-CoV-2', *The Lancet Infectious Diseases*, 2022.
[55] M Marovich et al, 'Monoclonal Antibodies for Prevention and Treatment of COVID-19', *JAMA*, 2020. **324**(2): p. 131-132.

cocktail of two monoclonal antibodies that target different sites on the spike protein to limit the emergence of drug resistant strains.[56] Despite these precautionary measures, some monoclonal antibodies have already been reported to have lost efficacy against the delta and omicron variants of concern.

Antiviral agents

Antiviral agents are a promising COVID-19 treatment option that can reduce disease severity, associated mortality and health system burden. Broad spectrum antivirals, have the potential to terminate replication in a wide range of viruses. However, most antivirals are specifically made to target one virus of interest. Antivirals such as Veklry (remdesivir) Lagevrio (molnupiravir) and Paxlovid (nirmatrelvir and ritonavir) prevent the progression of disease by targeting host cell pathways that support replication of the SARS-CoV-2 virus.[57]

Antivirals can be administered via multiple routes including as an intravenous infusion or in the form of an oral capsule or tablet. The latter is a significant benefit for the health system as patients can be treated at home without the need to use hospital resources compared to monoclonal antibodies which are intravenously administered in an in-patient or out-patient setting. Oral treatments are also administered more easily in hard-to-reach areas such as rural and remote regions. The prevention of viral replication by antivirals is also less likely to be hindered by emerging SARS-CoV-2 variants of concern, compared to monoclonal antibody therapies, as antivirals possess a high genetic barrier to the development of resistance.[58] Antiviral treatments are also more robust and scalable compared to monoclonal antibody treatments. However, antivirals are often linked with drug-drug interactions and pharmacokinetic contraindications.[59]

Efficacy of treatments against Omicron variants

A recent study published in the New England Journal of Medicine assessed the efficacy of several promising monoclonal antibodies and antiviral agents against the new omicron variants of concern (BA.1, BA.2, BA.4 and BA.5) using live-virus focus reduction neutralisation testing *in vitro*.[60]
The reference strain used in the study was SARS-CoV-2/UT-NC002–1T/Human/2020/Tokyo.

[56] F Han et al., 'Current treatment strategies for COVID-19 (Review)', *Mol Med Rep*, 2021. **24**(6): p. 858.
[57] M Tampere et al., 'Novel Broad-Spectrum Antiviral Inhibitors Targeting Host Factors Essential for Replication of Pathogenic RNA Viruses', *Viruses*, 2020. 12(12).
[58] B Malone and E.A. Campbell, 'Molnupiravir: coding for catastrophe', *Nature Structural & Molecular Biology*, 2021. **28**(9): p. 706-708.
[59] D Focosi et al., 'Monoclonal antibody therapies against SARS-CoV-2', *The Lancet Infectious Diseases*, 2022.
[60] E Takashita et al., 'Efficacy of Antibodies and Antiviral Drugs against Omicron BA.2.12.1, BA.4, and BA.5 Subvariants', *New England Journal of Medicine*, 2022. **387**(5): p. 468-470.

Table 1. Efficacy of Monoclonal Antibodies and Antiviral Drugs against Omicron Subvariants in Vitro.*

Subvariant	Mean Neutralization Activity of Monoclonal Antibody†								Susceptibility to Antiviral Drug‡		
	Imdevimab	Casirivimab	Tixagevimab	Cilgavimab	Sotrovimab Precursor	Bebtelovimab	Imdevimab+ Casirivimab	Tixagevimab+ Cilgavimab	Remdesivir	Molnupiravir	Nirmatrelvir
	ng per milliliter								μmol		
Reference§	7.4	6.1	6.1	7.0	95.1	2.5	3.4	6.3	1.7	2.8	2.7
BA.1	>50,000	>50,000	1552.7	2916.9	40727.1	5.8	>10,000	351.1	1.9	7.5	4.8
BA.1.1	>50,000	>50,000	603.5	>50,000	3769.2	3.9	>10,000	1296.8	2.0	6.0	3.9
BA.2	329.0	>50,000	2756.6	16.9	>50,000	3.3	835.1	34.6	5.9	8.7	6.9
BA.2.12.1	238.1	>50,000	335.2	21.0	>50,000	4.0	452.7	38.1	0.5	3.2	1.8
BA.4	132.6	>50,000	>50,000	53.6	>50,000	2.9	459.1	37.8	1.2	3.3	2.9
BA.5	583.4	>50,000	>50,000	56.8	>50,000	3.3	1093.1	192.5	2.0	4.1	4.4

Figure 9: Efficacy of monoclonal antibodies and antiviral drugs against omicron subvariants in vitro[61]

Results from the study demonstrated that Veklury (remdesivir), Paxlovid (nirmatrelvir and ritonavir), Lagevrio (molnupirivari) and bebtelovimab retained neutralising activity against all omicron strains including BA.4 and BA.5. Evusheld (tixagevimab + cilgavimab) demonstrated a significant drop in efficacy against BA.5 in comparison to BA.2 and the reference strain. Xevndy (sotrovimab) and Ronapreve (casirivimab with imdevimab) were found to be ineffective against the omicron strains.

The mean neutralisation activity of the monoclonal antibodies ($FRNT_{50}$) and the potency (IC_{50}) of antiviral agents against each strain tested is detailed in Figure 9 above. Findings from the study suggest that the selection of monoclonal antibodies to treat patients infected with omicron variants requires careful consideration.

[61] E Takashita et al., 'Efficacy of Antibodies and Antiviral Drugs against Omicron BA.2.12.1, BA.4, and BA.5 Subvariants', *New England Journal of Medicine*, 2022. **387**(5): p. 468-470.

Attachment 6: Additional information on the TGA

Provisional registration pathway

COVID-19 vaccines are eligible for provisional registration following review by the Therapeutic Goods Administration (TGA). This pathway involves a thorough review of the medicine by the TGA and is not an "emergency use authorisation".

To submit an application under the provisional registration pathway, a sponsor must first submit a provisional determination application. The TGA assesses the application against specific eligibility criteria, such as the nature of the clinical data, evidence of a plan to submit comprehensive clinical data obtained over a longer period, and the clinical need. If the TGA grants a provisional determination, the sponsor is then eligible to apply for provisional registration of the vaccine in the Australian Register of Therapeutic Goods (ARTG).

Once a provisional determination has been made, a sponsor must submit an application for provisional registration in the ARTG. This required a sponsor to submit a comprehensive dossier including specific information on clinical studies, non-clinical/toxicology studies, chemistry, manufacturing, risk management and other information.

Once an application is accepted, the TGA will commence a formal evaluation process that is carried out in multiple phases by technical experts. This process involves obtaining further information and clarification from the sponsor. For an application to be reviewed – *all* relevant data (including data from relevant phases of clinical trials) must be submitted to the TGA at the commencement of the evaluation.

The Advisory Committee on Vaccines (vaccines) or the Advisory Committee on Medicines (treatments) provide advice on applications. Both committees are comprised of Ministerially appointed independent experts.

Once an evaluation is complete, the TGA delegate (a senior medical officer) decides whether to grant provisional registration to the medicine. The decision to approve a new medicine is made on the basis that the benefits for a particular population outweigh the risks.

Once approved by the TGA, the medicine is included in the ARTG as a provisionally registered medicine and can be lawfully supplied in Australia by the sponsor.

The TGA will continue to play an active role in the ongoing monitoring of vaccines available in Australia and has robust procedures in place to investigate any potential new safety, quality or efficacy issues. The TGA's vaccine safety monitoring system is designed to detect, investigate, and respond to any emerging safety issues identified for COVID-19 vaccines. Post-market monitoring relies on reviewing and analysing adverse events reports, working with international regulators, and reviewing medical literature, media, and other potential sources of new safety information.

Emergency Use Provisions

Section 18A of the *Therapeutic Goods Act 1989* provides that the Minister may exempt specified therapeutic goods from the requirement to be included in the ARTG. The power may be exercised if the Minister is satisfied that, in the national interest, the exemption should be made so that the goods can be made available urgently in Australia to deal with an actual threat to public health caused by an emergency.

Exemptions such as these are exercised rarely and on the basis that safety, efficacy and quality may not be established with supply under this exemption, recognising that the TGA does not typically

have access to data on safety, efficacy and quality of the product. The provisional registration pathway has been the preferred method to enable access and protect safety.

Variations

Changes made to manufacturing processes of vaccines and treatments must be notified to/approved by the TGA.

Under rolling review processes for COVID-19 applications, and global manufacturing supply routes with multiple sites, products were subject to multiple variations following initial provisional registration. Variations included:

- Product Information (PI) document (adverse events)
- dosing and dosage form
- formulation
- manufacturing process and site changes

Large numbers of variations have been assessed for each vaccine including:

- Pfizer vaccine, COMIRNATY: 97 iterations plus 2 new products (each with their own changes) in 18 months
- AstraZeneca vaccine, VAXZEVRIA: 34 iterations in 18 months
- Moderna vaccine, SPIKEVAX: 23 iterations in <12 months, plus one new product
- Gilead treatment, remdesivir (VEKLURY): 12 iterations in 2 years
- GSK treatment, sotrovimab (XEVUDY): 11 iterations in <12 months

Collaboration with other bodies during the pandemic

The TGA collaborated with international regulators, leveraging knowledge gained via information and work sharing, but also contributing to the global body of regulatory knowledge.[1] Information-sharing was undertaken with the:

- Australia-Canada-Singapore-Switzerland-United Kingdom (Access) Consortium: The Access Consortium is a medium-sized coalition of regulatory authorities that work together to promote greater regulatory collaboration and alignment of regulatory requirements. Work and information was shared with the Consortium.
- European Medicines Agency (EMA) Open initiative and EMA Quality Working Group: The EMA launched a pilot 'OPEN' initiative in December 2020 to increase international collaboration on the evaluation of COVID-19 vaccines and therapeutics. Australia was one of four global regulators invited to participate in relevant EMA committee discussions.
- United States Food and Drug Administration (US FDA)
- Medsafe (the New Zealand Medicines and Medical Devices Safety Authority)
- WHO: Prequalification team: the WHO prequalification team works in close cooperation with national regulatory agencies and other partner organisations to make quality priority medical products available for those who urgently need them.
- International Coalition of Medicines Regulatory Authorities (ICMRA): ICMRA brings together the heads of 30 medicines regulatory authorities from every region in the world, with the World Health Organisation (WHO) as an observer. ICMRA shared information about manufacturing, vaccine confidence, and post-market surveillance.

[1] For further information: Therapeutic Goods Administration, COVID-19 vaccine: International collaboration, TGA, 16 September 2021, accessed 2 September 2022.

Attachment 7: Regulatory approval timeframes (international comparison)

Sponsor	Type	Name	TGA-Provisional registration effective date	FDA- Emergency use authorisation (EUA) date	EMA- Conditional approval date
Biocelect Pty Ltd on behalf of Novavax Inc	Protein vaccine	NUVAXOVID (NVX-CoV2373) a. For individuals aged 18 years and over b. Booster dose for individuals aged 18 years and over	 a. 19 Jan 22 b. 09 Jun 22	 a. 13 Jul 22 b. Not yet	 a. 20 Dec 21 b. Not yet
Moderna Australia Pty Ltd	mRNA	SPIKEVAX (elasomeran) a. For individuals aged 18 years and over b. For individuals aged 12 years and over c. Booster dose for individuals aged 18 years and over d. For individuals aged 6 years and over e. For individuals aged 6 months to less than 6 years	 a. 9 Aug 21 b. 3 Sept 21 c. 7 Dec 21 d. 17 Feb 22 e. 18 Jul 22	 a. 18 Dec 20 b. 17 Jun 22 c. 19 Nov 21 d. 17 Jun 22 e. 17 Jun 22	 a. 6 Jan 21 b. 23 July 21 c. 27 Oct 21 d. 24 Feb 22 e. Not yet
Janssen-Cilag Pty Ltd	Viral vector	COVID-19 Vaccine Janssen For individuals aged 18 years and over	25 Jun 21	27 Feb 21	11 Mar 21
AstraZeneca Pty Ltd	Viral vector	VAXZEVRIA (previously COVID-19 Vaccine AstraZeneca) a. For individuals aged 18 years and over b. Booster dose for individuals aged 18 years and over	 a. 15 Feb 21 b. 8 Feb 22	 a. Not yet b. Not yet	 a. 29 Jan 21 b. 24 May 22
Pfizer Australia Pty Ltd	mRNA	COMIRNATY (tozinameran) a. For individuals aged 16 years and over b. For individuals aged 12 years and over c. Booster dose for individuals aged 18 years and over d. For individuals aged 5 years and over e. Booster dose for individuals aged 16-17 years old f. Booster dose for individuals aged 12-15 years old	 a. 25 Jan 21 b. 22 Jul 21 c. 26 Oct 21 d. 3 Dec 21 e. 27 Jan 22 f. 7 Apr 22	 a. 11 Dec 20 b.10 May 21 c.22 Sept 21/19 Nov 21 d. 29 Oct 21 e. 8 Dec 21 f. 3 Jan 22	 a. 21 Dec 20 b. 28 May 21 c. 4 Oct 21 d. 25 Nov 21 e. 24 Feb 22 f. 24 Feb 22

Table 1: COVID-19 vaccines[1]

[1] TGA, COVID-19 vaccine: Provisional registrations, accessed 2 September 2022; FDA, COVID-19 Vaccines, accessed 2 September 2022; EMA, COVID-19 vaccines: authorised, accessed 2 September 2022.

Sponsor	Name	TGA-Provisional registration effective date	FDA- Emergency use authorisation (EUA) date	EMA- Conditional/approval date
AstraZeneca Pty Ltd	tixagevimab and cilgavimab (EVUSHELD) a. For pre-exposure prophylaxis in individuals 12 years and over	24 Feb 22	8 Dec 21	25 Mar 22
Merck Sharp & Dohm (Australia) Pty Ltd	molnupiravir (LAGEVRIO)	18 Jan 22	23 Dec 21	Not yet
Pfizer Australia	nirmatrelvir + ritonavir (PAXLOVID)	18 Jan 22	22 Dec 21	28 Jan 22
Celltrion Healthcare Australia Pty Ltd	regdanvimab (REGKIRONA)	6 Dec 21	Not yet	12 Nov 21
Roche Products Pty Ltd	tocilizumab (ACTEMRA)	1 Dec 21	24 Jun 21	6 Dec 21
Roche Products Pty Ltd	casirivimab + imdevimab (RONAPREVE)	15 Oct 21	21 Nov 20	12 Nov 21
GlaxoSmithKline Australia Pty Ltd	sotrovimab (XEVUDY)	20 Aug 21	26 May 21	7 Dec 21
Gilead Sciences Pty Ltd	remdesivir (VEKLURY) a. For treatment of COVID-19 in adults and adolescents (aged 12 years and weighing at least 40 kg) with pneumonia, requiring supplemental oxygen. b. For treatment of: •adults and paediatric patients (at least 4 weeks of age and weighing at least 3 kg) who have pneumonia due to SARS-CoV-2, who require supplemental oxygen •adults and paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at high risk of progressing to severe COVID-19	a. 10 July 20 b. 6 May 22	a. 22 Oct 20 b. 21 Jan 22	a. 3 July 20 b. 20 Dec 21

Table 2: COVID-19 treatments.[2]

[2] TGA, COVID-19 treatments: Provisional determinations, accessed 2 September 2022; FDA, Emergency Use Authorization, accessed 2 September 2022; EMA, COVID-19 treatments: authorised, accessed 2 September 2022.

Attachment 8: Policy timeline

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
2-Jul-20	Health Minister confirmed donation of Remdesivir to Australia.	Procurement	Treatment	Health Minister
6-Jul-20	Therapeutic Goods Administration (TGA) provides provisional determination for Gilead Sciences COVID-19 treatment remdesivir (Veklury).	Policy	Treatment	TGA
10-Jul-20	TGA provisional approval of first COVID-19 treatment Remdesivir (Veklury).	Policy	Treatment	TGA
13-Jul-20	Health Minister announced TGA provisional approval and purchase of Remdesivir.	Announcement	Treatment	Health Minister
19-Aug-20	Australia's COVID-19 Vaccine and Treatment Strategy released.	Policy	Whole Response	Department of Health
26-Aug-20	Australia announced it would support the Gavi COVAX Facility Advance Market Commitment (COVAX AMC) to improve access for Pacific and Southeast Asian countries to safe and affordable COVID-19 vaccines.	Policy	Whole Response	Foreign Minister, Health Minister and Minister for International Development and the Pacific
7-Sep-20	Prime Minister announced production and supply agreements to secure early access to vaccine doses with the University of Oxford/AstraZeneca (Oxford) and the University of Queensland/CSL (UQ) COVID-19 vaccines.	Procurement	Vaccine	Prime Minister
23-Sep-20	Australia joined the COVAX facility, enabling the purchase of COVID-19 vaccine doses as they become available.	Policy	Whole Response	Foreign Minister and Health Minister
5-Nov-20	Australian Government reached new COVID-19 vaccine agreements with Novavax Inc (40 million doses) and Pfizer/BioNTech (10 million doses).	Procurement	Vaccine	Health Minister
13-Nov-20	National Cabinet endorsed Australia's COVID-19 Vaccination Policy.	Policy	Whole Response	National Cabinet
11-Dec-20	Australian Government announced it had secured an additional 20 million doses of AstraZeneca (to be produced in Australia by CSL) and 11 million doses of Novavax.	Procurement	Vaccine	Health Minister
24-Dec-20	Australian Government announced that contracts had been signed with DHL Supply Chain and Linfox (for distribution and logistics), Accenture (tracking of vaccine doses and overall program implementation monitoring) and PwC (Program Delivery Partner).	Procurement	Vaccine	Health Minister
7-Jan-21	Australia's COVID-19 Vaccine National Rollout Strategy published. The Strategy outlined that all Australians who wished to be vaccinated would be able to do so in 2021, in the rollout phase that applied to them.	Policy	Whole Response	Health Minister
20-Jan-21	TGA granted a provisional determination to Biocelect Pty Ltd (on behalf of Novavax Inc) for COVID-19 vaccine, NVX-CoV2373.	Procurement	Vaccine	TGA
21-Jan-21	Australian Government announced it had appointed a panel of four providers (Aspen Medical, Healthcare Australia, International SOS and Sonic Clinical Service)	Procurement	Whole Response	Prime Minister

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	to supplement the existing immunisation workforce for specific populations.			
24-Jan-21	Australian Government announced General Practitioners (GPs) key role in the COVID-19 vaccination rollout and opened an expressions of interest process for accredited general practices.	Statement	Vaccine	Health Minister
25-Jan-21	TGA granted the Pfizer/BioNTech COVID-19 vaccine provisional approval for use in Australia in individuals 16 years and older.	Procurement	Vaccine	TGA
27-Jan-21	Communications campaign launched to provide timely, transparent and credible information to the Australian public on the COVID-19 vaccine program.	Communications	Vaccine	Health Minister
4-Feb-21	New legislation passed through Parliament, requiring all vaccination providers to report vaccinations to the Australian Immunisation Register (AIR), including information on COVID-19 vaccinations.	Policy	Vaccine	Parliament
4-Feb-21	Additional purchase of 10 million doses of Pfizer/BioNTech, bringing the total to 20 million doses through the Government's Advance Purchase Agreement with Pfizer.	Procurement	Vaccine	Health Minister
4-Feb-21	Australian Government extended access to COVID-19 vaccines to all visa-holders in Australia and announced an additional $1.3 million for communication activities to help reach culturally and linguistically diverse (CALD) communities.	Policy	Vaccine	Prime Minister
8-Feb-21	Release of the first Australian Government funded training modules for the COVID-19 vaccination workforce, including for immunisation providers and non-clinical and administration staff.	Procurement	Vaccine	Health Minister
14-Feb-21	Publication of the Government's Culturally and Linguistically Diverse Communities Implementation Plan.	Policy	Whole Response	Department of Health
s47, s47E, s34(3)				
16-Feb-21	TGA provisionally approved the Oxford/AstraZeneca COVID-19 vaccine for use in Australia, for individuals 18 years and older.	Procurement	Vaccine	TGA
16-Feb-21	Health Minister announced aged care residents in Australia would soon receive their first vaccine dose. The announcement included the intent for the aged care rollout to begin in every state and territory (including regional and rural aged care facilities) and take approximately six weeks.	Policy	Vaccine	Health Minister
18-Feb-21	Health Minister announced further details of the first stages of the program. The first phase of the vaccine rollout prioritised frontline health workers, quarantine and border workers, and aged care and disability workers and residents. Initial Pfizer hub locations were announced for 16 hub locations.	Policy	Vaccine	Health Minister
21-Feb-21	Prime Minister and Health Minister launched the COVID-19 vaccination program with an event at a health clinic in Sydney. The Prime Minister, Chief	Policy	Vaccine	Prime Minister/ Health Minister

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	Medical Officer and Chief Nursing and Midwifery officer also received a vaccine.			
22-Feb-21	Commencement of 1A roll out.	Milestone	Vaccine	N/A
24-Feb-21	Department of Health released a public statement in relation to the incorrectly administered vaccination in a Brisbane aged care facility.	Statement	Vaccine	Department of Health
28-Feb-21	Second phase of the Australian Government's $31 million public information campaign launched.	Communications	Whole Response	Health Minister
s47, s47E, s34(3)				
2-Mar-21	As part of the continued expansion of the Phase 1a COVID-19 vaccine rollout, it was announced that the Australian Defence Force would provide supplementary support to the rollout of vaccines to Australians in aged care.	Statement	Vaccine	Health Minister
6-Mar-21	Department of Health published updated advice on priority groups for COVID-19 Vaccination in Phase 1b.	Policy	Vaccine	Department of Health
7-Mar-21	Health Minister addressed reports that AstraZeneca doses expected from overseas had not been provided authorisation to proceed.	Statement	Vaccine	Health Minister
7-Mar-21	First doses of the Oxford AstraZeneca vaccine were administered. Recipients included aged care staff, Chief Medical Officer, and Health Minister.	Milestone	Vaccine	N/A
7-Mar-21	It was announced that more than 4,500 accredited general practices would participate in Phase 1b of Australia's COVID-19 rollout. More than 1,000 GPs would commence on 22 March 2021.	Policy	Vaccine	Health Minister
8-Mar-21	The Aboriginal and Torres Strait Islander Peoples Implementation Plan was published. This plan was developed in consultation with the Aboriginal and Torres Strait Islander Advisory Group on COVID-19, and with state and territory governments. $14.8 million will be provided to support the sector be vaccine ready.	Policy	Whole Response	Health Minister
14-Mar-21	Australian Government announced it was ramping up its campaign against misinformation on the COVID-19 vaccines and the Department of Health launched a new section on the website called 'Is it true?'	Policy	Vaccine	Prime Minister
17-Mar-21	Australian Government confirmed that more than 1,000 general practices would join the COVID-19 vaccination program from 22 March 2021. Services will come online from 22 March and progressively increase in number to more than 4,000 by the end of April – as part of Phase 1B. Over 100 Aboriginal Health Services and 130 Commonwealth operated GP-led Respiratory Clinics will also be progressively added as additional vaccine providers.	Statement	Vaccine	Health Minister
17-Mar-21	Australian Government announced the provision of 8,000 AstraZeneca COVID-19 vaccines to Papua New Guinea (PNG) from Australia's stock. These doses will enable vaccination PNG to vaccinate their essential health workforce.	Procurement	Vaccine	Prime Minister

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
22-Mar-21	Commencement of 1B roll out.	Milestone	Vaccine	N/A
23-Mar-21	TGA approved the first batches of the Australian made, CSL produced AstraZeneca vaccine.	Procurement	Vaccine	TGA
24-Mar-21	At the Winnunga Nimmityjah Aboriginal Health Service in Ngunnawal country in Canberra, local Ngunnawal elders received their first dose of the AstraZeneca vaccine along with the Minister for Indigenous Australians, the Shadow Minister for Indigenous Australians and Professor Tom Calma.	Milestone	Vaccine	N/A
28-Mar-21	Health Minister announced that over 500,000 COVID-19 vaccination doses had been administered across Australia.	Statement	Vaccine	Health Minister
13-Apr-21	TGA grants provisional determination to GlaxoSmithKline for the COVID treatment sotrovimab (Xevudy)	Policy	Treatment	TGA
4-Apr-21	Health Minister announced that the primary care presence for the vaccination rollout would increase to over 3,000 sites within the week and remains on track for over 4,000 sites to be on-board by the end of April.	Policy	Vaccine	Health Minister
8-Apr-21	Prime Minister, Health Minister, Chief Medical Officer and Secretary of the Department of Health announced the ATAGI recommendation that the Pfizer vaccine be preferred over the AstraZeneca vaccine for adults aged under 50 years. ATAGI considered the latest vaccination findings out of Europe and the UK – which followed extremely rare instances of people, having taken the AstraZeneca vaccine, developing a very specific syndrome involving blood clots with low platelet counts.	Policy	Vaccine	Prime Minister, Health Minister, ATAGI
s47, s47E, s34(3)				
9-Apr-21	Australian Government announced that over 1,000,000 COVID-19 vaccination doses had been administered across Australia.	Statement	Vaccine	Prime Minister
9-Apr-21	Prime Minister announced that the Australian Government had secured an additional 20 million doses of the Pfizer-BioNTech COVID 19 vaccine, in line with advice from the Science and Industry Technical Advisory Group led by Dr Murphy. Through the Government's Advance Purchase Agreement with Pfizer, these additional 20 million Pfizer doses means Australia will now receive a total of 40 million Pfizer doses in 2021.	Policy	Vaccine	Prime Minister/SITAG
22-Apr-21	Prime Minister announced that National Cabinet agreed to recalibrate the delivery model for the COVID-19 Vaccination Rollout Strategy, taking into account the ATAGI medical advice on the use of AstraZeneca vaccines, and COVID-19 vaccine supply arrangements by:	Policy	Vaccine	National Cabinet

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	• Limiting access to the Pfizer vaccine to those under 50 years and other specific circumstances. • Bringing forward phase 2a for people aged 50–69 years. • Increasing access to the Pfizer vaccine by immediately opening state and territory-operated sites to eligible people. • Allocating more doses of AstraZeneca to general practices. • Allowing states and territories to choose to incorporate community. pharmacies earlier into their roll-out plans in rural and remote areas where there are no or limited other points of presence.			
26-Apr-21	Department of Health's Vaccine Operations Centre (VOC) commenced publishing a Weekly Operational Update on the status of the vaccine rollout.	Communications	Vaccine	Department of Health
27-Apr-21	Health Minister and Minister for Senior Australians and Aged Care Services announced that National Cabinet agreed to vaccinate athletes and support staff headed to the Tokyo Olympic and Paralympic Games under priority group 1b.	Policy	Vaccine	Health Minister
3-May-21	Phase 2a of the roll out for over 50s commenced (GPRCs and state and territory vaccination clinics) commenced.	Milestone	Vaccine	N/A
5-May-21	Health Minister announced that the weekly number of doses of AstraZeneca being provided to general practices across Australia will increase. Participating general practices previously receiving 50 doses per week, will now receive 150 doses per week, and general practices receiving 100 doses per week, will now receive 200 doses per week.	Policy	Vaccine	Health Minister
13-May-21	Prime Minister announced that the Australian Government has secured 25 million doses of the Moderna COVID-19 vaccine to further diversify our vaccine portfolio. The agreement includes 10 million doses in 2021 and 15 million doses of Moderna's updated variant booster vaccine in 2022.	Procurement	Vaccine	Prime Minister
17-May-21	Phase 2a of the roll out for over 50s commenced.	Milestone	Vaccine	N/A
20-May-21	Health Minister and Queensland Health Minister announced community pharmacies in selected rural and regional areas will be activated to support Australia's COVID-19 vaccine rollout. Over the coming weeks, community pharmacies in rural and regional Queensland will be the first to be brought on board.	Policy	Vaccine	Health Minister and Qld Health Minister
25-May-21	ATAGI expanded its recommendations on the use of additional (booster) doses of COVID-19 vaccine	Policy	Vaccine	ATAGI
26-May-21	Australian Government released an additional 130,000 vaccines to support Victoria to accelerate vaccinations in the state, in response to a COVID-19 outbreak.	Procurement	Vaccine	Health Minister
27-May-21	Expressions of interest opened for up to 900 additional general practices to enrol in the COVID-19 vaccination program.	Milestone	Vaccine	Department of Health

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
3-Jun-21	Australian Government announced that they will contribute an additional $50 million to the COVAX Advance Market Commitment (COVAX AMC).	Statement	Whole Response	Prime Minister
4-Jun-21	Prime Minister announced that National Cabinet agreed that the COVID-19 vaccine eligibility would expand (in addition to individuals already eligible) to include: • All adults aged 40-49. • All Aboriginal and Torres Strait Islander people aged 16 to 49. • NDIS participants aged years 16 and over, and carers of NDIS participants of any age. • Temporary visa holders aged under 50 years who are currently in Australia and have been approved for return travel to Australia through the travel exemption process.	Policy	Vaccine	National Cabinet
4-Jun-21	Minister Hunt announced that residential aged care providers will be required to report the number of their staff vaccinated against COVID-19.	Policy	Vaccine	Health Minister
8-Jun-21	National Cabinet endorsed eligibility cohorts commenced.	Policy	Vaccine	National Cabinet
8-Jun-21	Prime Minister also appointed Lieutenant General John (JJ) Frewen DSC, AM, to be the head of the National COVID Vaccine Taskforce, known as Operation COVID Shield.	Statement	Vaccine	Prime Minister
11-Jun-21	Prime Minister announced that Australia will commit at least 20 million vaccine doses to a global G7 push to boost access to safe and effective COVID-19 vaccines and pandemic preparedness in developing countries.	Policy	Vaccine	Prime Minister
17-Jun-21	Australian Government accepted updated advice from ATAGI that the Pfizer vaccine be preferred for adults under the age of 60.	Policy	Vaccine	ATAGI
18-Jun-21	Health Minister and Minister for Immigration, Citizenship, Migrant Services and Multicultural Affairs launched the CALD COVID-19 Health Small Grants Fund. The $1.2 million Small Grants Fund, which opened on 21 June 2021, is being administered by the Federation of Ethnic Communities' Councils of Australia to support multicultural community groups to design and deliver grassroots COVID-19 Vaccine communication activities tailored to the needs of their communities.	Policy	Vaccine	Health Minister
28-Jun-21	Prime Minister announced that National Cabinet agreed to: • Mandate that at least the first dose of COVID-19 vaccine be administered by mid-September 2021 for all residential aged care workforce. • Establish a COVID-19 professional indemnity scheme to provide additional certainty to healthcare practitioners who are providing advice to people in relation to COVID-19 vaccination. • Endorse AHPPC advice to require vaccinations and testing for quarantine workers including those	Policy	Vaccine	National Cabinet

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	involved in transportation. • Make all quarantine workers and their household contacts eligible for COVID 19 vaccination.			
2-Jul-21	Health Minister announced the establishment of a COVID-19 Vaccine Claim Scheme to provide further assurance and confidence to patients and health professionals in the COVID-19 vaccine rollout.	Policy	Vaccine	Health Minister
2-Jul-21	Health Minister announced an $11 million grant program to support aged care workers to get vaccinated.	Policy	Vaccine	Health Minister
5-Jul-21	Health Minister announced more than 500 GPs around Australia were commencing the administration of the Pfizer vaccine, in addition to 62 Commonwealth Vaccination Clinics (CVCs) and 15 Aboriginal and Torres Strait Islander Community Controlled Health Services (ACCHS) who will also begin administering Pfizer from this week.	Policy	Vaccine	Health Minister
9-Jul-21	Prime Minister announced that National Cabinet: • Strongly encourages all disability support workers to get vaccinated against COVID-19 to protect their own health and the health of the people for whom they are caring. • Notes the AHPPC will consider evidence for mandatory vaccination for disability support workers in August 2021. • Notes in August 2021, the AHPPC will consider making it mandatory for disability support workers who support NDIS participants in high risk disability residential settings, to have had at least their first dose of COVID 19 vaccine by 31 October 2021.	Policy	Vaccine	National Cabinet
11-Jul-21	Australian Government launched a new advertising campaign, 'Arm Yourself', to encourage eligible Australians to be vaccinated against COVID-19.	Communications	Vaccine	Prime Minister
13-Jul-21	ATAGI reviewed its clinical advice in the setting of increasing community COVID19 cases in Australia. Notably, these recommendations include a preferred decreased interval of 4-8 weeks for the second dose of AstraZeneca, in outbreak settings.	Policy	Vaccine	ATAGI
2-Aug-21	Health Minister announced that the Australian Government has accepted ATAGI's updated recommendations, which include the following groups of children aged 12 to 15 be prioritised for the Pfizer vaccine: • Children with specified medical conditions that increase their risk of severe COVID-19, including severe asthma, diabetes, obesity, cardiac and circulatory congenital anomalies, neuro developmental disorders, epilepsy, immune compromised and trisomy 21. • Aboriginal and Torres Strait Islander children. • All children aged 12–15 years in remote communities, as part of broader community outreach	Policy	Vaccine	ATAGI

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	vaccination programs that provide vaccines for all ages (≥12 years).			
2-Aug-21	Health Minister announced in a press conference that from 9 August, children aged between 12 to 15 years old with specific medical conditions, who identify as Aboriginal and Torres Strait Islander or live in a remote community will be able to receive a Pfizer COVID-19 vaccine.	Policy	Vaccine	Health Minister
3-Aug-21	Doherty Report was released which advises on the National Plan to transition Australia's National COVID Response.	Milestone	Whole Response	N/A
6-Aug-21	Prime Minister announced that National Cabinet: • Noted to bring forward additional Pfizer vaccines in hotspot areas in respect of the current NSW and Queensland Hotspot areas. *Noting a separate request from Victoria had been received by Operation COVID Shield. • Received a briefing from the Solicitor General on the use of vaccinations in the workplace.	Policy	Vaccine	National Cabinet
6-Aug-21	Health Minister announced in a media release that the Australian government is supporting primary care COVID-19 vaccination providers to offer vaccinations to residential aged care and disability support workers through dedicated workplace-based clinics.	Policy	Vaccine	Health Minister
8-Aug-21	Health Minister announced in a media release that the Australian Government secured an initial shipment of over 7,700 doses of the novel monoclonal antibody treatment sotrovimab.	Procurement	Treatment	Health Minister
9-Aug-2021	TGA grants provisional determination to Merck Sharp & Dohme's antiviral COVID-19 treatment Molnupiravir (Lagevrio).	Policy	Treatment	TGA
9-Aug-21	Moderna COVID-19 vaccine was provisionally approved for use in Australians aged 18 years and over by the TGA.	Procurement	Vaccine	TGA
12-Aug-21	Health Minister announced in a media release that the Australian Government will provide an additional 7,680 Pfizer COVID-19 vaccine doses immediately for use in the eight affected local government areas, including Walgett.	Procurement	Vaccine	Health Minister
15-Aug-21	Prime Minister announced one million additional doses of the Pfizer vaccine had been secured from Poland.	Procurement	Vaccine	Prime Minister
17-Aug-21	In a press conference with the Prime Minister and the Foreign Minister, Minister Hunt announced that in response to the outbreak in western New South Wales: • The Government will be deploying ADF vaccination teams. • AUSMAT team is expected to be dispatched within 48 hours to provide clinical support to hospitals and Health services. • On-going work with the Royal Flying Doctors Service.	Policy	Whole Response	Prime Minister

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
20-Aug-21	TGA provisionally approves GlaxoSmithKline's COVID-19 treatment: sotrovimab (Xevudy)	Policy	Treatment	TGA
20-Aug-21	Health Minister announced purchase of, and TGA approval of, Sotrovimab doses.	Announcement	Treatment	Health Minister
20-Aug-21	TGA grants provisional determination to Roche Products for the COVID treatment casirivimab and imdevimab (Ronapreve).	Policy	Treatment	TGA
20-Aug-21	Prime Minister announced that those aged 16 -39 would be eligible for the Pfizer vaccine from 30 August. Bookings for these vaccinations will be occurring on 13 September. The eligibility check was updated on 30 August to reflect these changes.	Policy	Vaccine	Prime Minister
27-Aug-21	The Prime Minister announced after ATAGI advice that all children aged 12 – 15 years are eligible to receive the Pfizer vaccine.	Policy	Vaccine	ATAGI
30-Aug-21	Prime Minister announced that Australia has secured 500,000 doses of Pfizer from Singapore.	Procurement	Vaccine	Prime Minister
3-Sep-21	Health Minister, Foreign Minister and the Prime Minister announce that Four million extra Pfizer-BioNTech (Pfizer) vaccine doses will begin arriving in Australia in days following a historic partnership between the Australian and United Kingdom Governments.	Procurement	Vaccine	Prime Minister
4-Sep-21	Moderna (Spikevax) COVID-19 vaccine for adolescents aged 12 to 17 years provisionally approved by the TGA.	Procurement	Vaccine	TGA
9-Sep-21	ATAGI notes the TGA's registration of Pfizer and Moderna for use in children from 12 years of age. ATAGI now supports COVID-19 vaccination in all adolescents from 12 years of age.	Policy	Vaccine	ATAGI
12-Sep-21	Health Minister and LTGEN Frewen announce the launch of the next phase of the Australian Government's COVID-19 vaccination communications campaign.	Communications	Whole Response	Department of Health
13-Sep-21	Government announces increased allocations of Pfizer to GPs and state clinics in Victoria focusing on North West Melbourne.	Policy	Vaccine	Health Minister
14-Sep-21	Health Minister announces that the RfT is open for additional COVID-19 vaccination providers to begin the workplace vaccination program.	Policy	Vaccine	Health Minister
14-Sep-21	Health Minister announces in a press release that The Australian Government is further boosting the vaccination program for Aboriginal and Torres Strait Islander people across 30 priority areas to ensure all Australians can access a COVID-19 vaccine.	Policy	Vaccine	Health Minister
14-Sep-21	Department of Health announces that bookings are open for all people in Australia aged 12 years and over.	Statement	Vaccine	Department of Health
16-Sep-21	Health Minister announces in a press release that Aged care workforce leads the nation in vaccination uptake.	Statement	Vaccine	Health Minister
18-Sep-21	Health Minister announces in a press release that First million doses of Moderna arrive from Europe.	Procurement	Vaccine	Health Minister

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
22-Sep-21	Department of Health announces that Moderna vaccine is available in pharmacies.	Policy	Vaccine	Department of Health
23-Sep-21	A statement from ATAGI about the need for COVID-19 vaccine booster shots is released.	Statement	Vaccine	ATAGI
27-Sep-21	TGA grants provisional determination to Roche Products for COVID-19 treatment tocilizumab (Actemra).	Policy	Treatment	TGA
27-Sep-21	COVID-19 vaccination information kiosks are now open in shopping centres and at festivals in Queensland and Western Australia to help you book a vaccination appointment.	Milestone	Vaccine	Department of Health
30-Sep-21	An opinion piece from Professor Alison McMillan, Chief Nursing and Midwifery Officer on the positive vaccination rates among the aged care workforce is released.	Statement	Vaccine	N/A
1-Oct-21	Prime Minister releases a statement on the rates at which COVID19 vaccination levels would impact international travel.	Policy	Vaccine	Prime Minister
1-Oct-21	From 1 October 2021, all Australians aged 12 and over, including those Australians aged 60 and over, are now eligible to receive a Pfizer or Moderna COVID-19 vaccine. This means older Australians can now choose the Pfizer, Moderna, or AstraZeneca vaccine.	Policy	Vaccine	Department of Health
1-Oct-21	Health Minister announced people aged 60 years and over can access mRNA vaccines.	Policy	Vaccine	Prime Minister
1-Oct-21	A statement is released by AHPPC on the role of ventilation in reducing the risk of transmission of COVID-19 and an additional statement on COVID-19, schools and reopening Australia.	Statement	Whole Response	AHPCC
4-Oct-21	Government announces purchase of 300k Molnupiravir (Lagevrio).	Procurement	Treatment	Department of Health
5-Oct-21	TGA grants provisional determination to Pfizer for COVID-19 oral treatment nirmatrelvir and ritonavir (Paxlovid).	Policy	Treatment	TGA
5-Oct-21	Prime Minister announces that Australia will have access to an additional COVID-19 treatment following the Government's deal to purchase 300,000 courses of the oral COVID-19 treatment Molnupiravir.	Policy	Vaccine	Prime Minister
7-Oct-21	ATAGI releases a statement recommending a third dose of COVID-19 vaccines for people who are immunocompromised.	Policy	Vaccine	ATAGI
14-Oct-21	Health Minister announces in a press release that TGA has provided provisional determination to allow Pfizer to submit their application for the Pfizer vaccine to be administered to 5 to 11-year-olds.	Procurement	Vaccine	TGA
15-Oct-21	TGA grants provisional approval to Roche Products Pty Ltd COVID-19 treatment Ronapreve.	Policy	Treatment	TGA
17-Oct-21	Health Minister announced purchase of Ronapreve and Pfizer oral treatments.	Procurement	Treatment	Health Minister
21-Oct-21	TGA provisional approval for Ronapreve expanded to include the prevention of COVID-19 in patients of the same age and weight as for treatment who have been	Policy	Treatment	TGA

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	exposed to SARS-CoV-2 and who either have a medical condition making them unlikely to respond to or be protected by vaccination, who have not been vaccinated against COVID-19.			
27-Oct-21	TGA approval for Pfizer COVID-19 vaccine booster dose.	Procurement	Vaccine	TGA
28-Oct-21	Prime Minister announces booster shots for people who have been fully vaccinated for over 6 months, preferred vaccine being Pfizer, and Health Minister announces Pfizer will be available in pharmacies from 8 November.	Policy	Vaccine	Prime Minister
4-Nov-21	TGA grants provisional determination to AstraZeneca for the pre-exposure prophylaxis treatment tixagevimab and cilgavimab (Evusheld) for 18 years and older.	Policy	Treatment	TGA
8-Nov-21	Health Minister announces commencement of the COVID-19 booster vaccination rollout program, with the initial focus on residential aged care and disability facilities.	Policy	Vaccine	Health Minister
25-Nov-21	TGA grants provisional approval to Roche Products Pty Ltd COVID-19 treatment Ronapreve	Policy	Treatment	TGA
1-Dec-21	TGA grants provisional approval to Roche Products for COVID-19 treatment tocilizumab (Actemra).	Policy	Treatment	TGA
5-Dec-21	Health Minister announces that the TGA has provisionally approved the Comirnaty (Pfizer) vaccine as safe and effective for use among 5 to 11-year-old children in Australia, to start rolling out the Pfizer vaccine to this age group from 10 January 2022.	Policy	Vaccine	TGA
10-Dec-21	Prime Minister releases a statement that the Australian Government has accepted recommendations from ATAGI for the Comirnaty (Pfizer) vaccine to be made available to all children aged 5 to 11 years as one-third of the dosage given to people aged 12 years and over.	Policy	Vaccine	ATAGI
12-Dec-21	Health Minister announces ATAGI has approved Spicata (Moderna) as a COVID-19 booster shot for Australians aged 18 and over; and ATAGI has updated its advice and recommends booster doses be provided from five months after completion of the primary course of vaccination.	Policy	Vaccine	ATAGI
14-Dec-21	Prime Minister releases a statement concerning a new sovereign vaccine manufacturing facility to be built in Australia to produce respiratory mRNA vaccines for potential future pandemics and seasonal health issues as part of a new in-principle agreement between the Australian Government, Victorian Government and global mRNA company Moderna.	Policy	Vaccine	Prime Minister
16-Dec-21	$9.8 billion new investment in Australia's health care and COVID response (Evusheld announcement in MYEFO).	Announcement	Treatment	Health Minister
24-Dec-21	A statement from ATAGI has recommends reducing the minimum interval between the COVID-19 primary	Policy	Vaccine	ATAGI

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	vaccination course and the booster dose from 5 months to 4 months from 4 January 2022 or as soon as practical. Then as soon as possible, ATAGI recommends reducing the interval for boosters to a minimum of 3 months following the second dose of the primary course.			
s47, s47E, s34(3)				
4-Jan-22	TGA grants additional provisional determination for Evusheld as prophylaxis and treatments for people 12 years and older.	Policy	Treatment	TGA
17-Jan-22	ATAGI statement on severely immunocompromised children aged 5 to 11 years. Now recommended to receive a 3rd primary dose of COVID-19 vaccine, 2 to 4 months after their second dose, in line with other severely immunocompromised age cohorts.	Policy	Vaccine	ATAGI
17-Jan-22	ATAGI advise people aged 18 years or older who received a 3-dose primary course due to severe immunocompromise are now recommended to receive a booster (4th) dose ≥ 4 months after their 3rd dose.	Policy	Vaccine	ATAGI
18-Jan-22	TGA grants provisional approval to Pfizer for the oral COVID-19 treatment Paxlovid.	Policy	Treatment	TGA
18-Jan-22	TGA grants provisional approval to Merck Sharp & Dohme for the oral COVID-19 treatment Lagevrio.	Policy	Treatment	TGA
19-Jan-22	ATAGI provides advice on reduction of Temporary Medical Exemptions to 4 months following SARS-CoV-2 infection.	Policy	Vaccine	ATAGI
20-Jan-22	TGA has provisionally approved the first two oral antiviral COVID-19 treatments.	Announcement	Treatment	Health Minister
24-Jan-22	ATAGI provides recommendation on the use of the Novavax vaccine for those 18 years and older. Novavax is not recommended as a booster at present.	Policy	Vaccine	ATAGI
28-Jan-22	TGA provisionally approved the Pfizer COVID-19 vaccine, COMIRNATY, for use as a booster in individuals aged 16 and 17 years old.	Procurement	Vaccine	TGA
3-Feb-22	ATAGI recommends extending the booster program to 16 and 17 year olds, who can now receive a single dose of the adult Pfizer vaccine.	Policy	Vaccine	ATAGI
5-Feb-22	TGA grants provisional determination to Gilead Sciences for remdesivir for children.	Policy	Treatment	TGA
9-Feb-22	TGA provisionally approved a booster dose of the AstraZeneca (Vaxzevria) for individuals aged 18 years and older.		Vaccine	TGA
10-Feb-22	ATAGI released guidance on defining 'up-to-date' status for COVID-19 vaccination. All individuals aged 16 years and over are recommended to receive a COVID-19 vaccine booster dose to maintain an "up-to-date" status. This booster dose is now recommended from 3 months after the last primary dose. This is called the 'due date'. Children and adolescents aged 5-15 years are up-to-date after completion of a primary	Policy	Vaccine	ATAGI

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	course of vaccination. Severely immunocompromised individuals aged 5 years and over require a 3rd primary dose of a COVID-19 vaccine from 2 months (and no later than 6 months) after dose 2 to remain up-to-date.			
12-Feb-22	Health Minister and Minister for Senior Australians and Aged Care Services announced the Interim Guidance on Managing Public Health Restrictions on Residential Aged Care Facilities had been released based on expert medical advice from AHPPC.	Policy	Whole Response	Health Minister
15-Feb-22	AHPPC released a statement on mandating booster vaccinations in residential aged care workers.	Statement	Vaccine	AHPPC
17-Feb-22	TGA provisionally approved the Moderna (Spikevax) for a two-dose schedule of 50µg per dose in 6 to 11 year old children.	Procurement	Vaccine	TGA
23-Feb-22	ATAGI makes recommendation on the use of Moderna (Spikevax) COVID-19 vaccine in children aged 6 to 11 years.	Policy	Vaccine	ATAGI
24-Feb-22	TGA provisionally approves AstraZeneca's combination therapy (tixagevimab and cilgavimab (Evusheld) - for pre-exposure prevention (prophylaxis) of COVID-19.	Policy	Treatment	TGA
1-Mar-22	First COVID-19 oral antiviral treatment Lagevrio® (molnupiravr) listed on the PBS.	Announcement	Treatment	Health Minister
2-Mar-22	ATAGI makes updated recommendations on boosters. Nuvaxovid (Novavax) can be used as a booster in an individual aged 18 years and above if no other COVID-19 vaccine is considered suitable for that individual. AstraZeneca is now only recommended when there are medical contraindications to the mRNA vaccines.	Policy	Vaccine	ATAGI
16-Mar-22	AHPPC released a statement on mandating booster vaccination for disability support workers.	Statement		AHPPC
25-Mar-22	ATAGI makes recommendations on additional booster doses (referred to as a *winter dose*) for selected populations at the highest risk of severe illness from COVID-19. The dose is recommended for adults aged 65 years and older; residents of aged care or disability care facilities; people aged 16 years and older with severe immunocompromise; and Aboriginal and Torres Strait Island people aged 50 years and older.	Policy	Vaccine	ATAGI
29-Mar-22	Budget 2022 - Record investment in the future of Australia's health system	Announcement	Treatment	Health Minister
6-Apr-22	Published ATAGI advice on use of sedation for COVID-19 vaccination.	Policy	Vaccine	ATAGI
8-Apr-22	Published ATAGI statement on use of booster doses in adolescents aged 12-15 years.	Policy	Vaccine	ATAGI
10-Apr-22	Paxlovid® (nirmatrelvir and ritonavir) to be listed on the PBS as the second oral treatment from 1 May 2022.	Announcement	Treatment	Health Minister
28-Apr-22	Approval for updated ATAGI recommendations for Myocarditis following COVID-19 mRNA vaccines.	Policy	Vaccine	ATAGI
29-Apr-22	ATAGI updates recommended primary dose interval for mRNA vaccines (Pfizer and Moderna), and	Policy	Vaccine	ATAGI

Date	Announcement	Category	Vaccine/ Treatment	Decision Making/ Responsible Body
	Novavax. Primary doses of mRNA vaccines (Pfizer and Moderna) should be given at an interval of 8 weeks. The interval can be reduced to 3 weeks for Pfizer or 4 weeks for Moderna in specific circumstances. The primary dose interval for Novavax can also be extended from 3 weeks to 8 weeks.			
29-Apr-22	ATAGI updates recommended deferral time between a confirmed SARS-CoV-2 infection and a COVID-19 vaccine dose. All people are now recommended to defer COVID-19 vaccination after SARS-CoV-2 infection for 3 months.	Policy	Vaccine	ATAGI
25-May-22	ATAGI expanded its recommendations on the use of additional (booster) doses of COVID-19 vaccine.	Policy	Vaccine	ATAGI
9-Jun-22	ATAGI recommends a booster dose of Pfizer to 12-15 year olds who: are severely immunocompromised; have a disability with significant or complex health needs; have a complex and/or multiple health conditions that increase the risk of severe COVID-19.	Policy	Vaccine	ATAGI
7-Jul-22	ATAGI makes recommendations to expand access to the 4th dose of COVID-19 vaccines to people aged 30 or over, and to make the interval between SARS COV-2 infection or the previous dose of COVID-19 vaccine 3 months.	Policy	Vaccine	ATAGI
10-Jul-22	Eligibility for potentially lifesaving COVID-19 antiviral treatments will be widened from 11 July.	Announcement	Treatment	Health Minister
13-Jul-22	ATAGI advised that pregnant women aged 30 years and over are eligible to receive a second booster (also known as a fourth dose, and also known as a winter booster).	Policy	Vaccine	ATAGI
16-Jul-22	Medicare will cover a long consultation by a GP for the purpose of prescribing COVID-19 antivirals, with the change coming into effect from next week.	Announcement	Treatment	Health Minister
19-Jul-22	TGA provisionally approves Moderna COVID-19 vaccine (SPIKEVAX) for use in children from 6 months.	Procurement	Vaccine	TGA
22-Jul-22	The Australian Government has launched the latest phase of the COVID-19 campaign to inform Australians that COVID-19 oral antiviral treatments are available for eligible cohorts.	Announcement	Treatment	Department of Health and Aged Care
25-Jul-22	TGA provisionally approves the Biocelect Pty Ltd (Novavax) COVID-19 vaccine, NUVAXOVID, for use in individuals aged 12-17 years.	Procurement	Vaccine	TGA
17-Aug-22	The COVID-19 Vaccines and Treatments for Australia – Science and Industry Technical Advisory Group (SITAG) published summaries for COVID-19 vaccines and treatments for Australia.	Announcement	Treatment	SITAG
19-Aug-22	TGA grants provisional determination for COVID treatment sabizabulin.	Policy	Treatment	TGA

Attachment 9: AHPPH principles

Australian Government
Department of Health and Aged Care

Australian Health Protection Principal Committee (AHPPC)

The Australian Health Protection Principal Committee is the key decision-making committee for health emergencies. It is comprised of all state and territory Chief Health Officers and is chaired by the Australian Chief Medical Officer.

Role

The AHPPC has an ongoing role to advise the Australian Health Ministers' Advisory Council (AHMAC) on health protection matters and national priorities.

AHPPC is also tasked with the role of mitigating emerging health threats related to infectious diseases, the environment as well as natural and human made disasters.

The Committee works with states and territories to develop and adopt national health protection policies, guidelines, standards and alignment of plans.

AHPPC oversees 5 standing committees and one advisory group:

- Blood Borne Viruses & Sexually Transmitted Infections Standing Committee
- Communicable Diseases Network Australia
- Environmental Health Standing Committee
- National Health Emergency Standing Committee
- Public Health Laboratory Network of Australia
- Aged Care Advisory Group

Members

AHPPC is comprised of all state and territory Chief Health Officers and is chaired by the Australian Chief Medical Officer.

Contacts for the Chief Health Officers can be found on each state and territory's websites.

Attachment 10: SITAG Terms of reference

COVID-19 Vaccines and Treatments for Australia – Science and Industry Technical Advisory Group Terms of Reference

Role and purpose

To support the Australian Government to make decisions about purchasing and manufacture of COVID-19 vaccines and treatments the COVID-19 Vaccines and Treatments for Australia – Science and Industry Technical Advisory Group will provide advice on:

- the scientific validity of research into safety and efficacy of COVID-19 vaccine candidates
- potential purchase of COVID-19 vaccine candidates for Australia
- the scientific validity of research into new therapeutics for COVID-19, including tests and treatments
- potential purchase of COVID-19 therapeutics for Australia
- the viability of options for manufacturing and packaging COVID-19 vaccines and treatments in Australia
- distribution and logistics associated with COVID-19 vaccine candidates
- other technical matters related to COVID-19 vaccines and treatments, as requested by the Secretary, Department of Health or the Australian Government Chief Medical Officer.

Attachment 11: ATAGI Terms of reference

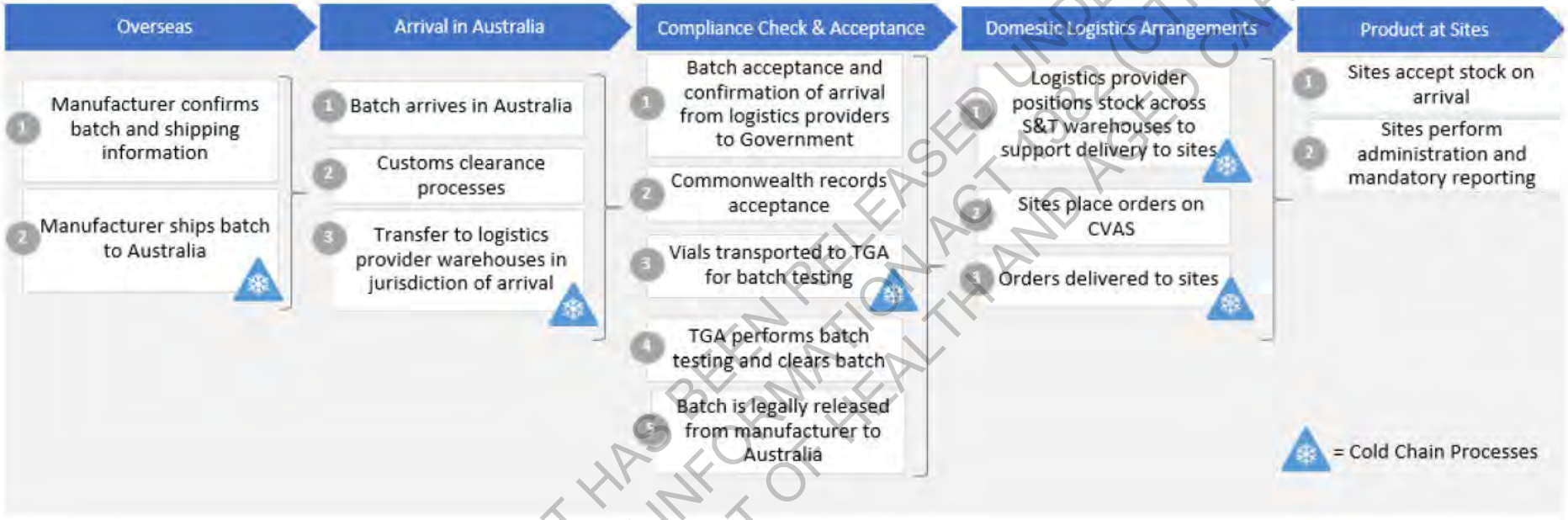
Australian Government
Department of Health

AUSTRALIAN TECHNICAL ADVISORY GROUP ON IMMUNISATION (ATAGI) | **TERMS OF REFERENCE**

THE TERMS OF REFERENCE OF THE AUSTRALIAN TECHNICAL ADVISORY GROUP ON IMMUNISATION ARE TO:

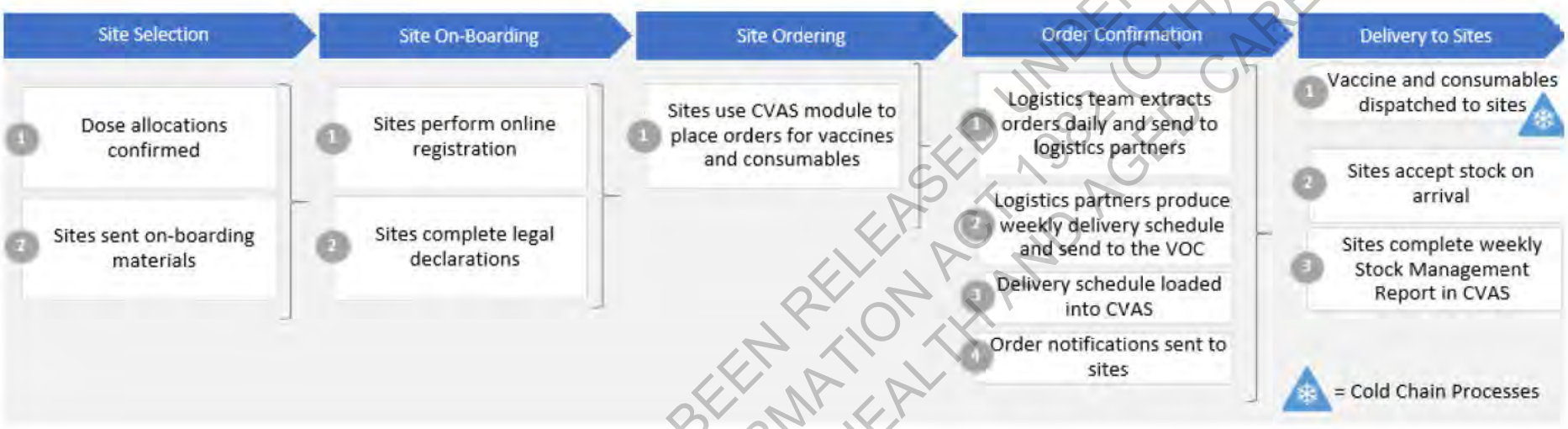
- provide technical advice to the Minister for Health on the medical administration of vaccines available in Australia, including those on the National Immunisation Program
- through the department, provide advice to research funding bodies regarding the status of current immunisation research and areas where additional research is required
- advise the Pharmaceutical Benefits Advisory Committee on matters relating to the ongoing strength of evidence pertaining to existing, new and emerging vaccines in relation to their effectiveness and use in Australian populations
- produce the Australian Immunisation Handbook for the approval of the National Health and Medical Research Council
- consult with the National Immunisation Committee (NIC) on the content and format of the Australian Immunisation Handbook and associated implementation strategies
- consult with the Communicable Diseases Network Australia (CDNA) and the Advisory Committee on Vaccines (ACV) on matters relating to the implementation of immunisation policies, procedures and vaccine safety

Attachment 13: Logistics and distribution process



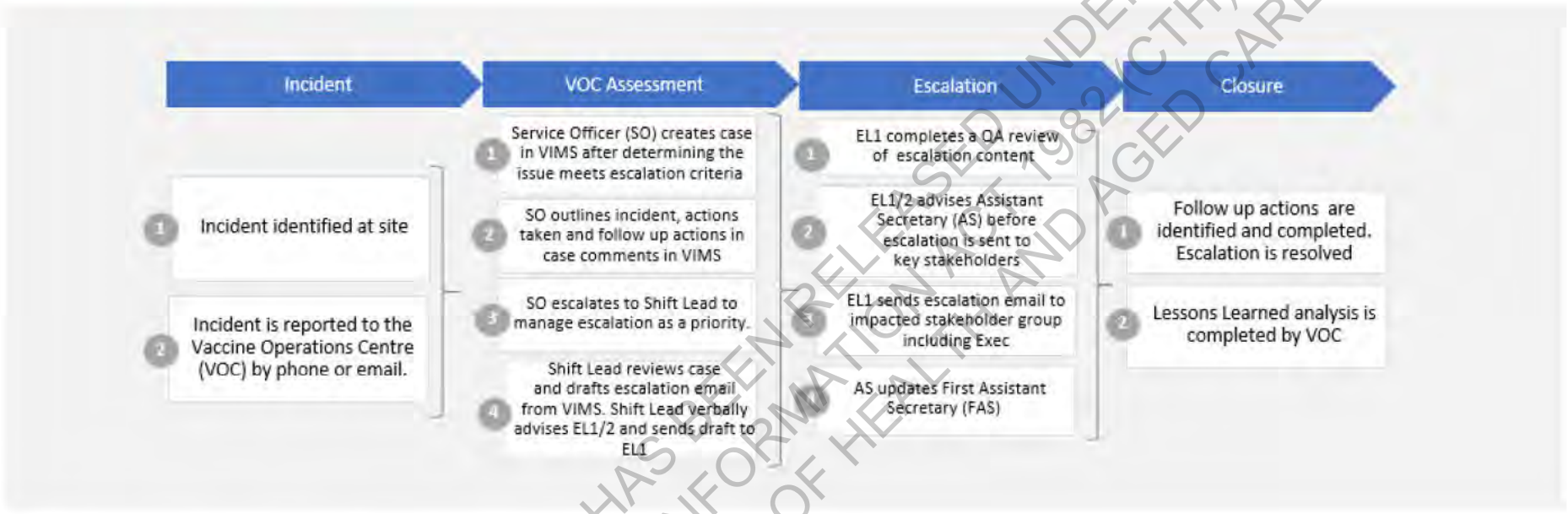
Source: Based on information provided by the Department of Health and Aged Care , 1 September 2022

Attachment 14: CVAS vaccine and consumables ordering process



Source: Based on information provided by the Department of Health and Aged Care , 1 September 2022

Attachment 15: Incident management escalation process



*Criteria to escalate an incident:

- Significantly impacts the day-to-day business of the COVID-19 vaccine rollout
- Significantly impacts the health and safety of staff or customers
- Significantly impacts the reputation of the Department
- Significantly impacts a community or region, including an emergency event
- Likely to be subject to enquiry or scrutiny by the media
- Is politically sensitive
- Has been sent to media/Ombudsman/Minister

Source: Based on information provided by the Department of Health and Aged Care, 13 September 2022

Attachment 16: TGA approved indications and ATAGI recommendations for use

The tables below outline the Therapeutic Goods Administration (TGA) indications and Australian Technical Advisory Group on Immunisation (ATAGI) recommendations for COVID-19 vaccines. The information is accurate as at 5 September 2022.[1]

VAXZEVRIA - AstraZeneca	
TGA approved indication	ATAGI recommendations for use
a. For individuals aged 18 years and over	•Pfizer, Moderna, or Novavax COVID-19 vaccines are preferred over AstraZeneca for people aged under 60 years. •AstraZeneca is not preferred in pregnancy. Pregnant women who have already received a first dose of AstraZeneca can receive an mRNA COVID-19 vaccine, AstraZeneca, or Novavax for their second dose. •The AstraZeneca COVID-19 vaccine is not preferred but can be used for the third dose in adults if there are contraindications to mRNA and Novavax COVID-19 vaccines.
b. Booster dose for individuals aged 18 years and over	•Although not preferred, AstraZeneca or Novavax COVID-19 vaccines can be used as a booster dose in people aged 18 years and older in the following circumstances: •people who have a contraindication to mRNA vaccines (including those who have had a serious adverse event following mRNA vaccines, such as a history of anaphylaxis or myocarditis attributed to an mRNA vaccine) •people who do not prefer an mRNA vaccine

COMIRNATY - Pfizer	
TGA approved indication	ATAGI recommendations for use
a. For individuals aged 16 years and over b. For individuals aged 12 years and over	•Pfizer, Moderna, or Novavax COVID-19 vaccines are preferred over AstraZeneca for people aged under 60 years. •mRNA COVID-19 vaccines (Pfizer or Moderna) are the recommended vaccines in pregnancy. There are substantial data on their safe use in pregnancy. •An mRNA COVID-19 vaccine (Pfizer or Moderna) or the Novavax COVID-19 vaccine is recommended for the third dose. •Pfizer and Moderna COVID-19 vaccines are registered for use in people aged 12 years or older. •mRNA vaccines (Pfizer or Moderna) are the recommended COVID-19 vaccines for pregnant women.
c. Booster dose for individuals aged 18 years and over	•For people aged 18 years and older, Pfizer or Moderna COVID-19 vaccines are the preferred vaccines for a booster dose, regardless of which vaccine was used for the primary course.
d. For individuals aged 5 years and over	•The paediatric formulation of Pfizer COVID-19 vaccine is registered for use in children aged 5 to 11 years. It is preferable to complete the primary course with the same brand of vaccine, rather than a different brand.
e. Booster dose for individuals aged 16-17 years old f. Booster dose for individuals aged 12-15 years old	•For people aged 12 to 17 years, Pfizer COVID-19 vaccine is the only vaccine registered for use as a booster.

SPIKEVAX - Moderna	
TGA approved indication	**ATAGI recommendations for use**
a. For individuals aged 18 years and over b. For individuals aged 12 years and over	•Pfizer, Moderna, or Novavax COVID-19 vaccines are preferred over AstraZeneca for people aged under 60 years. •mRNA COVID-19 vaccines (Pfizer or Moderna) are the recommended vaccines in pregnancy. There are substantial data on their safe use in pregnancy. •An mRNA COVID-19 vaccine (Pfizer or Moderna) or the Novavax COVID-19 vaccine is recommended for the third dose. •Pfizer and Moderna COVID-19 vaccines are registered for use in people aged 12 years or older. •mRNA vaccines (Pfizer or Moderna) are the recommended COVID-19 vaccines for pregnant women.
c. Booster dose for individuals aged 18 years and over	•For people aged 18 years and older, Pfizer or Moderna COVID-19 vaccines are the preferred vaccines for a booster dose, regardless of which vaccine was used for the primary course.
d. For individuals aged 6 years and over	•The Moderna COVID-19 vaccine is registered for use in children and is available in a paediatric formulation. It is preferable to complete the primary course with the same brand of vaccine, rather than a different brand.
e. For individuals aged 6 months to less than 6 years	•The Moderna COVID-19 paediatric formulation (blue cap vial, 100 µg/mL) is the only vaccine available for use in this age group.
NUVAXOVID - Novavax	
TGA approved indication	**ATAGI recommendations for use**
a. For individuals aged 18 years and over	•Pfizer, Moderna, or Novavax* COVID-19 vaccines are preferred over AstraZeneca for people aged under 60 years. •An mRNA COVID-19 vaccine (Pfizer or Moderna) or the Novavax COVID-19 vaccine is recommended for the third dose. There is very limited evidence of the efficacy of Novavax in immunocompromised people. •mRNA COVID-19 vaccines (Pfizer or Moderna) are the recommended vaccines in pregnancy. There are substantial data on their safe use in pregnancy. Novavax COVID-19 vaccine can also be used in pregnancy.
b. Booster dose for individuals aged 18 years and over	•Although not preferred, AstraZeneca or Novavax COVID-19 vaccines can be used as a booster dose in people aged 18 years and older in the following circumstances: opeople who have a contraindication to mRNA vaccines (including those who have had a serious adverse event following mRNA vaccines, such as a history of anaphylaxis or myocarditis attributed to an mRNA vaccine) opeople who do not prefer an mRNA vaccine
Off-label	•Although not TGA-registered as a booster in this age group, Novavax can be used as a booster in people aged 12 years or older if no other COVID-19 vaccine brand is suitable for that person.
COVID-19 Vaccine Janssen - Janssen	
TGA approved indication	**ATAGI recommendations for use**
a. For individuals aged 18 years and over	No recommendations for use.

1. ATAGI, *Clinical recommendations for COVID-19 vaccines*, accessed 5 September 2022

Attachment 17: International Comparison on COVID-19 Treatments

Access to COVID-19 treatments in Australia is broadly comparable with access in other countries. Internationally comparable countries (Germany, Italy, Canada, South Korea, England, the United States (US) and New Zealand) are making COVID-19 treatments available for high-risk patients.

The majority of countries surveyed have made Lagevrio (molnupiravir) and Paxlovid (nirmatrelvir and ritonavir) available to COVID infected individuals in the community who are at higher risk of developing severe disease requiring hospitalisation and Veklury (remdesivir) available for use in hospitalised patients. To a smaller extent Evusheld (tixagevimab with cilgavimab) is available for pre-exposure prophylaxis (PrEP).[1]

s47, s47E, s34(3)

The mechanisms through which different jurisdictions provide access to treatments to higher risk patients in the community is variable, likely reflecting differences in local health systems.

Country	Medicines	Prescribing/supply	Distribution	Total courses	Courses per 100,000 population
Australia	Paxlovid, Lagevrio	Prescription only	PBS and states and territories	Paxlovid: 77,189[2] Lag: 243,4262	1,248
Canada	Paxlovid	Variable by province	Information Not available	Information Not available	-
New Zealand	Paxlovid, Lagevrio	Prescription and directly through some pharmacies	Community pharmacy	Information Not available	-
England	Paxlovid, Lagevrio	Specialist prescription only	Direct supply to identified at risk patients, Panoramic study	Total: 111,0003[3]	209
United States	Paxlovid, Lagevrio	Prescription and directly through some pharmacies	States and territories, test-to-treat centres	Paxlovid: 4,489,325[4] Lag: 673,8114	1,567

Table 1: Summary of available information on community antiviral distribution and uptake in select countries.

The National Health Service (NHS) in England provides direct access to oral antivirals for high-risk immune compromised individuals. These individuals were digitally identified and provided with rapid antigen tests. On recording a positive test result they are put on a care pathway, assessed by a clinician and if appropriate, provided with antiviral treatment to take at home. Around 85,000 people have accessed treatment this way. Other, nonimmune compromised higher risk patients are encouraged to access treatment via the Panoramic trial, with over 26,000 people enrolled to date.

[1] Department of Health, 2022, Survey of published studies from information Belgium, France, Germany, Italy, Canada, Israel, Korea South, New Zealand, Singapore, United Kingdom and United States undertaken 6-11 July 2022, supplemented with verbal updates provided by Canada, New Zealand, United Kingdom and United States on 18 August 2022.
[2] DoHA 2022, Utilisation data from PBS and NMS 3 February to 4 September 2022, provided 9 September 2022.
[3] NHS 2022, Informal advice provided by NHS England on 18 August 2022.
[4] US HHS, COVID-19 Therapeutics Thresholds, Orders, and Replenishment by Jurisdiction, Utilisation data from 17 December to 4 September 2022, accessed 9 September 2022.

The US procures treatments at a federal level and provides them to states and territories for local distribution. The US has also created a "test to treat" program. Through this program, people can be tested and – if they are positive and treatments are appropriate for them – receive a prescription from a health care provider (either on site or through telehealth), and have their prescription filled all at one location. These "One-Stop Test to Treat" sites are available nationally at pharmacy-based clinics, federally funded health centres, long-term care facilities, and community-based sites.[5]

Access to, and use of, monoclonal antibody medicines for treatments, or PrEP, is more variable internationally. Casirivimab with imdevimab (Ronapreve) and sotrovimab (Xevudy) are no longer widely used because of concerns about effectiveness against some, or all, of the omicron variants.[6] Bebtelovimab, a MAB which retains *in-vitro* activity against omicron BA.4 and BA.5 is available only in the US. The reported US price for bebtelovimab is roughly double the US Lagevrio and Paxlovid prices.

Evusheld is the only monoclonal antibody with an indication for PrEP against COVID-19 which is being utilised. Access to Evusheld and the recommended dosage varies internationally. In Canada, some provinces such as British Columbia, are not providing access to Evusheld. In August 2022, the NHS announced England has decided to not procure Evusheld at this time due to concerns about efficacy and dosing again the omicron variants. The United States has purchased over 800,000 150-150 mg doses, equivalent to 240 doses per 100,000 population, with around half of these doses administered to patients and with monthly usage declining, notwithstanding that on 29 June, the US Food and Drug Administration approved a four-fold dose increase (from 150-150 mg once, to 300-300 mg every 6 months).

[5] US HHS 2022, Test to Treat, accessed 20 August 2022.
[6] D Yamasoba et al., 'Neutralisation sensitivity of SARS-CoV-2 omicron subvariants to therapeutic monoclonal antibodies', *Lancet Infect Dis*, 2022. **22**(7): p. 942-943.

Attachment 18: TGA, CET and PBS indications for use

The tables below outline the current Therapeutic Goods Administration (TGA) indications, National COVID-19 Clinical Evidence Taskforce (CET) recommendations and Pharmaceutical Benefits Scheme (PBS) eligibly criteria for COVID-19 Treatments. The information is accurate as at 2 September 2022.

Ronapreve (casirivimab + imdevimab) – Treatment of Mild-Moderate COVID-19	
TGA Approved Indication	**CET Recommendations for Use**
On 15 October 2021, the TGA provisionally approved Ronapreve for the treatment of COVID-19 in adults and adolescents aged 12 years and older and weighing at least 40 kg who do not require supplemental oxygen for COVID 19 and who are at increased risk of progressing to severe COVID-19. Ronapreve should be administered as soon as possible after a positive viral test for SARS CoV 2 and not later than 7 days after the onset of first symptoms.	The CET provides conditional recommendation to consider using Ronapreve in adults and children including pregnant or breastfeeding women with COVID-19, within seven days of symptom onset, who do not require oxygen and who have one or more risk factors for disease progression. Do not use Ronapreve in individuals hospitalised with moderate-to-critical COVID 19. Where Omicron is likely to be the dominant circulating variant, use of Ronapreve should only be considered where other treatments are not suitable or available.

Ronapreve (casirivimab + imdevimab) – Post Exposure Prophylaxis	
TGA Approved Indication	**CET Recommendations for Use**
Ronapreve has received provisional approval for the prevention of COVID-19 in adults and adolescents aged 12 years and older and weighing at least 40 kg who have been exposed to SARS-CoV-2 and who either have a medical condition making them unlikely to respond to or be protected by vaccination, who have not been vaccinated against COVID 19. Ronapreve is not intended to be used as a substitute for vaccination against COVID-19.	The CET outlines consensus recommendations to consider using Ronapreve as prophylaxis in seronegative or polymerase chain reaction-negative close household contacts of individuals with confirmed COVID-19. Where Omicron is likely to be the dominant circulating variant, use of Ronapreve as post-exposure prophylaxis is unlikely to be effective and should only be used in exceptional circumstances.

Sources:
Therapeutic Goods Administration
Australian National COVID-19 Clinical Evidence Taskforce
Pharmaceutical Benefits Scheme

Lagevrio – Treatment of Mild-Moderate COVID-19		
TGA Approved Indication	**CET Recommendations for Use**	**PBS Eligibility Criteria**
Approved for the treatment of COVID-19 positive adults within five days of symptom onset who do not require initiation of oxygen due to COVID-19 and who are at increased risk for hospitalisation or death. The use of Lagevrio is not recommended in pregnancy and breastfeeding. It is recommended that sexually active women of childbearing potential use contraception and men also use contraception during and 3 months after treatment with Lagevrio.	CET provide a consensus recommendation for Lagevrio to use within 5 days of symptom onset in unvaccinated adults with COVID-19 who do not require oxygen and who: •have one or more risk factors for disease progression, and •where other treatments (such as Veklury or Paxlovid) are not suitable or not available. Do not use Lagevrio in pregnant or breastfeeding women, children and adolescents outside of randomised trials with appropriate ethical approval.	Eligibility for a PBS-subsided prescription of Lagevrio is limited to people with COVID 19: •aged 70 years or older, •aged 50 years or older with two or more risk factors for severe disease •aged 30 years, who identify as Aboriginal or Torres Strait Islander with and two or more risk factors for severe disease •aged 18 years or older who at risk of progressing to severe disease due to their immunocompromised status.

Paxlovid – Treatment of Mild-Moderate COVID-19		
TGA Approved Indication	**CET Recommendations for Use**	**PBS Eligibility Criteria**
TGA has approved Paxlovid for the treatment of COVID 19 positive adults within five days of symptom onset who do not require initiation of supplemental oxygen due to COVID-19 and are at increased risk of progression to hospitalisation or death. The use of Paxlovid is not recommended in pregnancy or breastfeeding, and in women of childbearing potential. It is recommended that sexually active women of childbearing potential use contraception. Paxlovid must also not be used with a number of other commonly used medicines. The list of medicines is outlined in the Product Information. Paxlovid must also not be used in patients with severely reduced kidney or liver function.	CET provide a consensus recommendation for the use of Paxlovid within 5 days of symptom onset in adults with COVID-19 who do not require oxygen and: •are immunosuppressed or not immunocompetent regardless of vaccination status; or •have received one or two doses of vaccine and who are at high risk of severe disease on the basis of age and multiple risk factors. •in exceptional circumstances, for the treatment of COVID 19 within 5 days of symptom onset in children and adolescents aged 12 years and over and weighing at least 40 kg who do not require oxygen and who are at high risk of deterioration OR; •in children and adolescents who are not up-to-date with vaccination, or who are immunosuppressed regardless of vaccination status. Do not use Paxlovid routinely in children and adolescents who are up-to-date with vaccination unless immunosuppressed. It is also not recommended in in pregnant or breastfeeding women outside of randomised trials with appropriate ethical approval.	Eligibility for a PBS-subsided prescription of Paxlovid is limited to people with COVID 19: •aged 70 years or older, •aged 50 years or older with two or more risk factors for severe disease, •aged 30 years, who identify as Aboriginal or Torres Strait Islander with and two or more risk factors for severe disease, •aged 18 years or older who at risk of progressing to severe disease due to their immunocompromised status.

Veklury (remdesivir) – Treatment of Moderate-Severe COVID-19	
TGA Approved Indication	**CET Recommendations for Use**
On 10 July 2020 the TGA approved Veklury for use in adults and adolescent (aged 12 and older) with severe COVID-19 symptoms who have been hospitalised. On 6 May 2022, the TGA extended the provisional approval for Veklury as a three-day treatment for mild-moderate disease paediatric patients (at least 4 weeks of age and weighing at least 3kg) who have pneumonia due to SARS CoV-2, who require supplemental oxygen	The CET provides a conditional recommendation for the use of Veklury: •in adults hospitalised with COVID-19 who require oxygen but do not require non-invasive or invasive ventilation •In pregnant or breastfeeding women hospitalised with COVID-19 who require oxygen but who do not require non-invasive or invasive ventilation. In addition, the CET lists a consensus recommendation for the use of Veklury within seven days of symptom onset under exceptional circumstances, children and adolescents aged 28 days or older and weighing at least 3kg who are hospitalised with severe COVID-19 (considered likely to progress to ventilation), who require systemic corticosteroids and oxygen but do not require non-invasive or invasive ventilation, where other treatments are not available / appropriate. Do not use Veklury in individuals with COVID-19 that require non-invasive or invasive ventilation.

Veklury (remdesivir) – Treatment of Mild-Moderate COVID-19	
TGA Approved Indication	**CET Recommendations for Use**
On 6 May 2022, the TGA extended the provisional approval for Veklury as a three-day treatment for: •mild-moderate disease in adults and paediatric patients (at least 4 weeks of age and weighing at least 3kg) who have pneumonia due to SARS-CoV-2, who require supplemental oxygen, and •adults and paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at high risk of progressing to severe COVID-19.	The CET provides a conditional recommendation for the use of Veklury in unvaccinated adults and pregnant women with COVID-19, within seven days of symptom onset, who do not require oxygen and who have one or more risk factors for disease progression. In addition, the CET lists a consensus recommendation for the use of Veklury within seven days of symptom onset for: •Adults with COVID-19 who do not require oxygen and are immunocompromised regardless of vaccination status; or who are not up-to-date with vaccination and who are at high risk of severe disease on the basis of age and multiple risk factors. •Under exceptional circumstances, children and adolescents aged 28 days and over and weighing at least 3kg who do not require oxygen and are at high risk of deterioration, where other treatments are not available / appropriate. Do not use Veklury in individuals with COVID-19 that require non-invasive or invasive ventilation.

Evusheld (tixagevimab and cilgavimab) – Pre-Exposure Prophylaxis for COVID-19	
TGA Approved Indication	**CET Recommendations for Use**
On 24 February 2022, the TGA granted provisional approval for the pre-exposure prophylaxis of COVID-19 in people aged 12 years and older weighing at least 40kg: •who have moderate-to-severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments that make it likely that they will not mount an adequate immune response to COVID 19 vaccination; or •for whom vaccination is not recommended due to a history of severe adverse reaction to a COVID-19 vaccine or COVID 19 vaccine component. The recommended dosage is 300mg of Evusheld administered as two separate 1.5 mL, sequential injections of: •150mg of tixagevimab •150mg of cilgavimab Evusheld is not recommended as a substitute for vaccination in individuals for whom COVID 19 vaccination is recommended.	The CET provides a conditional recommendation for use of Evusheld: •do not routinely use as pre-exposure prophylaxis, however use may be considered in exceptional circumstances, in individuals who are severely immunocompromised. Do not use Evusheld for the treatment of COVID-19 outside of randomised trials with appropriate ethical approval in: •adults who require mechanical ventilation •children under 12 years of age without risk factors for deterioration who do not require oxygen •for post-exposure prophylaxis for people exposed to SARS-CoV-2.

Evusheld (tixagevimab and cilgavimab) – Treatment of Mild-Moderate COVID-19	
TGA Approved Indication	**CET Recommendations for Use**
Not approved by the TGA. Use would be considered "off label" use.	The CET provides a conditional recommendation for use of Evusheld: •within five days of symptom onset in unvaccinated adults with COVID-19 who do not require oxygen and who have one or more risk factors for disease progression. •within 12 days of symptom onset in unvaccinated adults with COVID-19 who require oxygen but not invasive mechanical ventilation. The CET outlines consensus recommendations for Evusheld: •Use within five days of symptom onset in adults with COVID-19 who do not require oxygen and: oare immunocompromised regardless of vaccination status; or owho are not up-to-date with vaccination and who are at high risk of severe disease on the basis of age and multiple risk factors. •Use within 12 days of symptom onset in adults with COVID-19 who require oxygen and: oare immunocompromised; or oare at particularly high risk of severe disease on the basis of advanced age and multiple risk factors. •Use in exceptional circumstances for the treatment of COVID-19 within five days of symptom onset in children and adolescents aged 12 years and over and weighing at least 40kg who do not require oxygen and who are at high risk of deterioration. •Use in children and adolescents who are not up-to-date with vaccination, or those who are immunosuppressed regardless of vaccination status.

Xevudy (sotrovimab) – Treatment of Mild-Moderate COVID-19	
TGA Approved Indication	**CET Recommendations for Use**
On 20 August 2021, the TGA provisionally approved Xevudy for the treatment of adults and adolescents (aged 12 years and over and weighing at least 40kg) with COVID-19 who do not require initiation of oxygen due to COVID 19 and who are at increased risk of progression to hospitalisation or death. Xevudy should not be used in patients hospitalised due to COVID-19. Due to recent reports of reduced in vitro activity of Xevudy in against some omicron variants (BA.2, BA.4 and BA.5), the TGA has included a special warning in its product information sheet to note the uncertainty around if the approved dose of Xevudy will be effective against emerging variants.	The CET published conditional recommendations for the use of Xevudy: •to treat COVID-19 within five days of symptom onset in adults, including pregnant women in second or third trimester, who do not require oxygen and who have one or more risk factors for disease progression. •within five days of symptom onset in unvaccinated adults with COVID-19 who do not require oxygen and who have one or more risk factors for disease progression. The CET also made consensus recommendations for the use of Xevudy: •within five days of symptom onset in adults with COVID-19 who do not require oxygen and are immunocompromised regardless of vaccination status; or who are not up-to-date with vaccination and who are at high risk of disease on the basis of age and multiple risk factors. •in exceptional circumstances, to treat COVID19 within five days of symptom onset in children and adolescents aged 12 years and over and weighing at least 40kg who do not require oxygen and who are at high risk of deterioration. Where infection with Omicron BA.2 is confirmed or considered likely, use of Xevudy should only be considered where other treatments are not suitable or available. Do not use Xevudy routinely outside of randomised trials with appropriate ethical approval for the treatment of COVID-19 in children and adolescents under 12 years of age and without high risk factors for deterioration.

Actemra (tocilizumab) – Treatment of Moderate-Severe COVID-19	
TGA Approved Indication	**CET Recommendations for Use**
On 1 December 2022, the TGA provisionally approved Actemra for the intravenous treatment of confirmed COVID 19 in hospitalised adults aged 18 years and older who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. Actemra should not be used during pregnancy unless clearly necessary.	The CET provides a conditional recommendation for the treatment of COVID 19 using Actemra in adults including pregnant or breastfeeding women, children and adolescents who require supplemental oxygen, particularly where there is evidence of systemic inflammation.

Attachment 20: Potential future COVID-19 treatments

Bebtolovimab (LYCoV1404) by Eli Lilly, AbCellera

Bebtolovimab is a fully human recombinant neutralising immunoglobulin G-1 (IgG1 variant) monoclonal antibody consisting of two identical light chain polypeptides composed of 215 amino acids each and two identical heavy chain polypeptides composed of 449 amino acids produced by a Chinese hamster ovary cell line. Bebtolovimab works by binding to the spike protein of the virus that causes COVID-19.

Three studies using *in vitro* assays reported that bebtelovimab continues to retain neutralisation activity against emerging Omicron variants, including BA.4 and BA.5 in comparison to wildtype (B.1).[1]

A phase II randomised clinical trial called BLAZE-4 is evaluating the safety and efficacy of bebtelovimab treatment in non-hospitalised subjects with mild-to-moderate COVID-19 (at least one mild symptom) within 3 days of COVID-19 diagnosis.

The key findings from the trial were:

- In the low-risk patient group, persistently high viral load (PHVL) occurred 19.8 percent of patients in the placebo group compared to 12 percent of the patients treated with bebtelovimab leading to a 40 percent relative risk reduction.
- Reduction in viral load relative to placebo was also seen on Day 5 after treatment.
- Time to sustained symptom resolution was reduced by a median of 2 days for patients treated with bebtelovimab compared to placebo.
- The incidence of COVID-19-related hospitaliation or all-cause deaths by day 29 were similar within the low-risk population treated with bebtelovimab alone (n=2/125) in comparison to the placebo control group (n=2/128).

The majority of the adverse events reported were considered mild or moderate in severity.

On 11 Feb 2022, FDA issued an Emergency Use Authorisation (EUA) for bebtelovimab (LYCoV1404; LY3853113) to treat COVID-19.[2]

The EUA for bebtelovimab is for the treatment of mild to moderate COVID-19 in adults and paediatric patients (12 years of age and older weighing at least 40kg) with a positive COVID-19 test who are at high risk for progression to severe COVID19, including hospitalization or death, and for those whom alternative COVID-19 treatment options approved or authorized by the FDA are not accessible or clinically appropriate.

The authorized dosage of bebtelovimab is 175mg administered as an intravenous injection over at least 30 seconds. Bebtelovimab is not authorised for patients hospitalised due to COVID-19 or

[1] D Yamasoba et al., 'Neutralisation sensitivity of SARS-CoV-2 omicron subvariants to therapeutic monoclonal antibodies', *Lancet Infect Dis*, 2022. 22(7): p. 942-943; Y Cao et al., 'BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection', *Nature*, 2022. 608(7923): p. 593-602; Q Wang et al., 'Antibody evasion by SARS-CoV-2 Omicron subvariants BA.2.12.1, BA.4, and BA.5', *bioRxiv*, 2022: p. 2022.05.26.493517.

[2] US Food and Drug Administration, 'EUA Letter of Authorization Eli Lilly Bebtelovimab Emergency Use Authorization', *FDA,* 05 August 2022, accessed 16 August 2022.

require oxygen therapy due to COVID-19. On 16 June 2022, the FDA revised its factsheet to indicate that bebtelovimab retains activity to Omicron subvariants BA.2.12.1 and BA.4/BA.5.[3]

s47, s47E, s34(3)

Sabizabulin by Veru Inc.

Sabizabulin is a first-in-class oral medication that is a cytoskeleton disrupter with a dual mechanism of action. As an antiviral, sabizabulin binds to and inhibits microtubules (alpha and beta microtubulin) of the SARS-CoV-2 spike protein that are necessary for the virus to cause infection. Further, the inhibition of the alpha and beta microtubulin subunits by sabizabulin also achieves an anti-inflammatory effect, which could be beneficial in treating the cytokine storm included by SARSCoV-2.

A Phase 3 clinical trial of hospitalised high-risk patients with moderate to severe COVID-19 reported that those treated with sabizabulin (9mg once daily for up to 21 days) showed a 55.2 percent relative reduction in mortality.[4] s47, s47E, s34(3)

On 19 August the TGA issued a provisional determination for sabizubulin.[5] s47, s47E, s34(3)

Pegylated interferon lambda by Eiger Biopharmaceuticals

Interferons are made by the innate immune system in response to viral infections to stimulate expression of antiviral, antiproliferative, and immunoregulatory genes to help clear the infection.[6] While there are a few types of interferons, interferon lambda was thought to be ideal for investigation as a COVID-19 antiviral. This is because it is highly expressed in selected areas of the body such as epithelial cells in the lung, liver, and intestine, resulting in fewer systemic side effects and, was shown to be supressed during SARS-CoV-2 infection.[7]

Pegylated interferon lambda is a long-acting form of interferon lambda which can be used to maximise treatment effects. When pegylated interferon lambda is administered to a COVID-19 patient, it increases the expression of key antiviral, antiproliferative, and immunoregulatory genes that can combat the SARS-CoV-2 infection. The large number of genes induced by interferons is

[3] US Food and Drug Administration, 'Bebtelovimab Health Care Provider Fact Sheet', *FDA, 16 June 2022,* 16 August 2022.
[4] KG Barnette et al., 'Oral Sabizabulin for High-Risk, Hospitalized Adults with Covid-19: Interim Analysis', *NEJM* Evidence. **0**(0): p. EVIDoa2200145.
[5] TGA, COVID-19 treatments: Provisional determinations, *TGA,* 22 August 2022, accessed 28 August 2022
[6] A Park and A. Iwasaki, 'Type I and Type III Interferons - Induction, Signaling, Evasion, and Application to Combat COVID-19', *Cell Host Microbe*, 2020. 27(6): p. 870-878.
[7] L Prokunina-Olsson et al., 'COVID-19 and emerging viral infections: The case for interferon lambda', *J Exp Med*, 2020. 217(5) and P Jagannathan et al., 'Peginterferon Lambda-1a for treatment of outpatients with uncomplicated COVID-19: a randomized placebo-controlled trial', *Nature Communications*, 2021. 12(1): p. 1967.

expected to reduce the potential emergence of resistant SARS-CoV-2 strains.[8] Interferons are thought to be an optimal candidate for use as a COVID-19 antiviral.

The Phase 3 TOGETHER study evaluated the effectiveness of pegylated interferon lambda in non-hospitalised adult patients (majority vaccinated with at least one dose) with COVID-19, at high risk of progressing to severe illness. Data from the study demonstrated that treatment with pegylated interferon lambda significantly reduced the risk of COVID-19-related hospitalisations or emergency room visits greater than six hours by 50 percent and death by 60 percent. Reports of adverse events were similar between the control and treatment arms of the study, with the most commonly reported event being injection site reaction. The primary endpoint was achieved across all variants tested, including the early strains of omicron.[9]

A small phase two study (n=30) of adult outpatients treated with pegylated interferon lambda (single subcutaneous 180µg peginterferon lambda injection) within 7 days of symptom onset showed accelerated viral decline by day 7, particularly in those with high baseline viral load.[10]

s47, s47E, s34(3)

Amubarvimab (BRI196) with romlusevimab (BRI198) by Brii Biosciences

Amubarvimab (BRII-196) with romlusevimab (BRII-198) is a combination anti-SARS-CoV-2 monoclonal antibody that binds non-competitively to the ACE2 receptor to reduce viral binding to the host cell.[11] The structure of this antibody combination has also been engineered to allows for a long half-life of activity in plasma to allow for a longer lasting treatment effect.

In the ACTIV-2 phase 3 clinical trial, non-hospitalised adults at high risk for clinical progression were treated with a single dose of amubarvimab with romlusevimab (sequential infusion of 1000mg each). Results showed an 80 percent reduction in hospitalisation and death with fewer deaths through 28 days in the treatment arm compared to the placebo group. The safety outcomes reported were also improved in non-hospitalised COVID-19 patients at high risk of clinical progression to severe disease in comparison to the placebo group. The rate of efficacy in patients who commenced treatment early (0-5 days) vs late (6-10 days), following symptom onset was similar, confirming that this treatment could be used in patients who present late for treatment.[12]

This monoclonal antibody combination has been approved for use in China since December 2021 for adults at greater disease progression risk. The treatment has also been conditionally approved for use in adolescents aged 12 – 17 years of age. The company has also filed for emergency use authorisation in the US.

[8] JJ Feld et al., 'Peginterferon lambda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomised trial', *The Lancet Respiratory Medicine*, 2021. **9**(5): p. 498-510.
[9] Eiger BioPharmaceuticals Inc., '*Eiger's Single-dose Peginterferon Lambda for COVID-19 Reduced Risk of Hospitalization or ER Visits by 50% in a Predominantly Vaccinated Population in Phase 3 TOGETHER Study*', *prnewswire.com,* 17 March 2022, accessed 18 August 2022.
[10] JJ Feld et al., 'Peginterferon lambda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomised trial', *The Lancet Respiratory Medicine*, 2021. **9**(5): p. 498-510.
[11] A Garcia-Lledo et al., 'Pharmacological treatment of COVID-19: an opinion paper', *Rev Esp Quimioter*, 2022. 35(2): p. 115-130.
[12] TH Evering et al., 'LB2. Safety and Efficacy of Combination SARS-CoV-2 Monoclonal Neutralizing Antibodies (mAb) BRII-196 and BRII-198 in Non-Hospitalized COVID-19 Patients', *Open Forum Infect Dis,* 04 December 2021, 8(Suppl 1):S807-8.

On July 26, 2022, the company announced that the amubarvimab with romlusevimab combination retains neutralising activity against the new omicron variants BA.4 and B.5 based on a live virus study undertaken by the University of Maryland.[13]

s47E, s34(3)

Ensitrelvir (S-217622) by Shionogi Inc.

Ensitrelvir is an orally bioavailable 3CL protease enzyme inhibitor, similar to Paxlovid (nirmatrelvir and ritonavir). Ensitrelvir suppresses the replication of SARS-CoV-2 by selectively inhibiting 3CL protease.

A phase II/III clinical trial of mostly vaccinated patients with no risk factors for severe disease progression within 5 days of symptom onset were treated with ensitrelvir one a day for five days. Study results reported that ensitrelvir cleared the SARS-CoV-2 virus from the host rapidly and reduced viral shedding by 1-2 days in comparison to the placebo group. The proportion of patients with a positive viral titer was also significantly reduced by 90 percent by day four when compared to the control group. The drug was well-tolerated, with no reports of serious adverse events or death. Mild-moderate adverse events reported which resolved without the need for treatment.[14]

Ensitrelvir shows high *in vitro* antiviral activity against the Omicron subvariants BA.4 and BA.5 with similar to its potency against other existing variants.[15]

s47E, s34(3)

[13] Brii Biosciences, *Brii Biosciences Announces Positive Data Demonstrating its Long-Acting COVID-19 Neutralizing Antibody Therapy, Amubarvimab/Romlusevimab Combination* [media release], 27 July 2022, accessed 18 August 2022.
[14] Shionogi Inc, 'New Data for Shionogi's COVID-19 Once-Daily Oral Antiviral S-217622 Show Rapid Virus Clearance', *Shiongi Inc,* 23 April 2022, accessed 18 August 2022.
[15] Shionogi Inc, 'S-217622, a Therapeutic Drug for COVID-19, Shows High In Vitro Antiviral Activity Against Omicron Subvariants BA.4 And BA.5' 14 July 2022, accessed 18 August 2022.

Attachment 22: Influenza vaccine and NIP arrangements

The National Immunisation Program (NIP) is a joint initiative of the Commonwealth, state and territory governments, funded through the National Partnership on Essential Vaccines (NPEV).

The Commonwealth is responsible for vaccine purchases, system oversight, and provision of infrastructure such as the Australian Immunisation Register (AIR). State and territory governments are responsible for coordination and oversight of immunisation service delivery, distribution of vaccines, and public health activities such as responding to outbreaks of vaccine preventable diseases.

The NIP provides free essential vaccinations for a range of diseases. Influenza vaccination is included for free under the NIP for Medicare card holders who meet the eligibility criteria. Eligibility for a free vaccine is determined by the Pharmaceutical Benefits Advisory Council (PBAC) following clinical advice provided by the Australian Technical Advisory Group on Immunisation (ATAGI):

Cohort	Comments
6 months and over with certain medical risk factors	This includes anyone who has: •heart disease •severe asthma (requiring frequent medical consultations or use of multiple medications) •chronic lung conditions •diseases of the nervous system which affect your breathing •impaired immunity •diabetes •kidney disease •haemoglobinopathies •children aged six months to 10 years on long-term aspirin therapy
All children 6 months to less than 5 years	None
All Aboriginal and Torres Strait Islander people 6 months and over	None
65 years and over	None
Pregnant women	Any trimester during each pregnancy

Table 1: eligibility for free influenza vaccines under the NIP.[1]

s47C, s34(3)

The Commonwealth determines the quantity of vaccines to be ordered in October, with delivery of vaccines beginning in March the following year. The states and territories then order and distribute the vaccines to vaccine providers, including General Practice (GPs) and pharmacies. The high-level process is outlined at Figure 1 below.

In addition to the influenza vaccines available under the NIP, there is a significant private market for influenza vaccines that are available to the public. These vaccines are ordered from wholesalers in September in the previous year. No prescription is required to attend a pharmacy and receive an influenza vaccine. However, individuals who do not meet the NIP eligibility criteria must pay for their vaccine from the private market and an administration fee may also be charged. Many employers fund in-house vaccinations or provide reimbursement to employees.

[1] Provided by Department of Health and Aged Care, data as at 27 August 2022.

Figure 2: high level NIP supply chain.[2]

The proportion of influenza vaccinations procured by the private market relative to the NIP has also increased, indicating a growing interest in vaccination by less vulnerable individuals. The vaccine supply provided by the NIP and the private market from 2015 to 2022 (to 1 September 2022) is shown in Figure 2.

In 2022, all states and territories (excluding NT) made influenza vaccination free to all residents to ease pressure on the health system which was already struggling with COVID-19 patients. In addition, marketing materials were designed to encourage the simultaneous uptake (coadministration) of COVID-19 vaccine boosters and fourth doses. This was intended to lessen the impact of respiratory illnesses, including influenza and COVID-19, on the economy, health, and education systems. Further, providing influenza vaccines free of charge aimed to protect a population that had not been exposed to influenza over the previous two years due to increased social distancing and mask wearing.

The uptake of influenza vaccines has been increasing over recent years. Influenza vaccines are primarily administered via GPs but are also administered at pharmacies and other sites. This growth is likely due to the emergence of COVID-19 heightening public awareness of the potential impacts of respiratory disease.

[2] Provided by Department of Health and Aged Care, 11 August 2022.
[3] Provided by Department of Health and Aged Care, data as at 2 September 2022.