COVID-19 vaccines: Frequently asked questions

Q1. What types of vaccines are researchers developing?

Researchers are using a variety of methods to develop COVID-19 vaccines, some of which are well-established and some newer.

Established technologies use either the whole virus or parts of the virus (usually proteins) to train the immune system to recognise it. These technologies include:

- **inactivated vaccines**, where the whole virus is inactivated with chemicals or heat so that it cannot replicate
- **subunit vaccines**, where only a component of the virus is used, such as a protein
- **live attenuated vaccines**, which contain a weakened version of the virus. There are currently no live attenuated COVID-19 vaccines in clinical trials.

Newer technologies used in the development of COVID-19 vaccines use the genetic code for a component of the SARS-CoV-2 virus, usually the spike protein or the part of it called the receptor binding domain. After vaccination, host cells take up the genetic code and manufacture that protein, which then triggers an immune response. These technologies include:

- **DNA and mRNA vaccines**, which are molecules that contain genetic information (genes). These technologies have been under development for decades. However, there have not yet been any DNA or mRNA vaccines registered for use in humans.
- **Viral vector vaccines** in which a chemically weakened harmless virus like a common cold adenovirus (the vector) is used to carry the genetic code for the spike protein from SARS-CoV-2. There are currently two licensed viral vector vaccines for humans, both for the Ebola virus. Viral vectors are also used in licensed gene therapy products.

Q2. How are COVID-19 vaccines being tested?

Before a vaccine is registered for use, it is tested extensively during development and then in thousands of people. Testing first begins with laboratory research, then animal studies and finally human clinical trials.

Clinical trials involve testing the vaccine in volunteers, and are conducted in phases:

- Phase 1 clinical trials usually include a few dozen healthy adult volunteers and focus primarily on assessing safety, and also on demonstrating that the vaccine induces an immune response
- Phase 2 clinical trials have hundreds of volunteers, and can include groups for whom the new vaccine is intended, for example, older adults, children or people with pre-existing medical conditions. These trials aim to show the vaccine induces an immune response and confirm that it is safe with acceptable side effects.
- Phase 3 clinical trials include many thousands of participants and aim to show that a vaccine has efficacy (i.e. it is effective) in preventing people from getting the disease – in this case COVID-19. Phase 3 trials also thoroughly assess the vaccine for safety and side effects. In a phase 3 trial, researchers usually compare vaccinated people with people who received a placebo (like a salt water injection). They compare the rate of disease, disease severity and reported side effects between the two groups.

For COVID-19 vaccines, some of these phases have been combined. For example, in phase 1/2 trials, results are analysed after the first few dozen volunteers are studied, then the trial proceeds in hundreds more. Also, some phase 3 studies have started once preliminary data from phase 1/2 trials are available. Having these ‘overlapping’ time frames has helped develop COVID-19 vaccines quickly and help make them available earlier to save lives.

Q3. Why are clinical trials sometimes paused and restarted?

COVID-19 vaccine trials, in the same way as other vaccine clinical trials, are supervised by independent Data and Safety Monitoring Boards (also known as DSMBs). DSMBs can advise to pause or stop a trial if there are any safety events, such as a participant experiencing a severe illness or event that needs time to investigate more fully. This standard procedure is one of the important ‘checks and balances’ in clinical trials. Pausing a trial allows researchers to investigate the event and see if it may have been a side effect related to the vaccine or if it is coincidental. Since clinical trials usually include tens of thousands of participants and continue for many months, it is inevitable that some participants will experience unrelated illnesses during the trial.

If researchers are concerned that the vaccine is causing unacceptable side effects, they can stop the trial. This has not yet happened for any COVID-19 vaccine trials.

Q4. What is the process for getting a COVID-19 vaccine approved in Australia?

The Therapeutic Goods Administration (TGA), part of the Australian Government Department of Health, is the organisation responsible for approving medicines and vaccines for use in Australia. Approved products are listed on the Australian Register of Therapeutic Goods. The TGA receives advice from an independent panel of experts on the Advisory Committee on Vaccines. The approval process involves a rigorous assessment of vaccine effectiveness and safety. Given the urgency of the pandemic, the TGA is prioritising COVID-19 vaccines via a faster pathway which involves the following steps:

Provisional determination

Being granted provisional determination means that a vaccine developer is eligible to proceed to apply for provisional registration from the TGA. It does not mean that provisional approval has been granted, but that the vaccine can be assessed by the TGA using the provisional registration pathway.

As of 26 November, the TGA has granted provisional determination to three companies for their COVID-19 vaccines:

- AstraZeneca Pty Ltd, for the University of Oxford vaccine
- Pfizer Australia Pty Ltd, for the Pfizer/BioNTech vaccine
- Janssen Cilag Pty Ltd, for the Janssen vaccine

Provisional approval

The provisional approval pathway is a process that allows for temporary registration of promising new medicines and vaccines where the need for early access outweighs any potential risks. The decision to grant provisional registration is based on a number of factors, including:

- the safety, quality and effectiveness of the vaccine has been satisfactorily established for its intended use
- the sponsor's plan to submit comprehensive clinical data before the provisional registration ends.

After provisional approval, the TGA will continue to closely monitor any new data about the vaccine as it becomes available. Similar processes are used by regulatory authorities in other countries, such as the United States Food and Drug Authority and the European Medicines Agency.

Q5. How is vaccine safety monitored after a vaccine is approved for use?

After any vaccine is registered and it starts to be given to people, vaccination experts and regulators continue to monitor vaccine safety in several ways. People can report side effects or adverse events directly to the regulatory body, the TGA. This is called passive surveillance because it waits for people to report. As a further check, the TGA assesses the quality of every batch of vaccine before it can be supplied in Australia.

There is also active surveillance where researchers or regulators actively seek out any side effects in large groups of people given the vaccine. One form of active surveillance is where researchers continue to study the vaccine's effectiveness and safety (sometimes called 'phase 4' trials). Another form is using established systems such as AusVaxSafety, in which clinics send SMS messages to people receiving vaccines (or their parents or carers) to ask if they had any reactions after receiving a vaccine. Independent experts analyse the responses to make sure that any safety issues are detected quickly. AusVaxSafety operates in almost 300 clinics around Australia and cover hundreds of thousands of people.

The systems described above will be used and expanded to monitor vaccine safety for all licensed COVID-19 vaccines, with experts meeting to review all reported data even more frequently than for usual vaccines.

Q6. Why are COVID-19 vaccines being developed so quickly?

As of 26 November 2020, over 1.3 million people have died from COVID-19, and more than 8,000 are dying each day. In Australia, 907 people have died so far. Hundreds of millions of people are suffering from the ongoing social and economic devastation caused by the pandemic. The urgency of this crisis means that all available resources and efforts are being directed towards finding an effective vaccine.

Developing and licensing a vaccine has in the past taken a decade or longer, but some COVID-19 vaccines may be registered and used within 12–18 months of the virus being discovered.

Some of the reasons behind this rapid progress include:

- Unprecedented funding and collaboration between vaccine developers and governments around the world. Financial risks have been taken, such as building manufacturing facilities before a vaccine is even available.

- Technology has evolved to make vaccine development faster than in the past. Previously, viral vaccines could only be developed after growing the virus in a lab, which takes time. Newer technologies build vaccines using the genetic code for the virus, so researchers around the world were able to start their work as soon as the genome for the virus was released in January 2020.

Clinical trials progress more quickly if a disease is widespread, as is the case with COVID-19 in many countries, as a significant difference between the unvaccinated and vaccinated groups can be detected sooner than for a rare disease.

Q7. Are shortcuts being taken in vaccine safety assessment?

No. Although COVID-19 vaccine trials have been set up much more quickly than would have previously been possible, this does not mean that safety assessment has been compromised.

In fact most of the vaccines being developed have now included tens of thousands of people in their trials, totalling nearly one quarter of a million people being involved in trials altogether. This is actually providing a larger amount of data than for many other vaccines routinely used (see also Q2).

Each country has its own processes for assessing and monitoring the safety of vaccines. In Australia, any COVID-19 vaccine must meet the same high standards of the TGA as any other vaccine. Vaccine safety remains the TGA's top priority. COVID-19 vaccines will be prioritised, and more resources will be allocated to their assessment.

Q8. Which COVID-19 vaccines are likely to be used in Australia?

The Australian Government currently has four purchasing agreements for the supply of COVID-19 vaccines. These agreements will only go ahead if the vaccines are shown to meet acceptable standards of effectiveness and safety in clinical trials, and receive regulatory approval from the Therapeutic Goods Administration. As of 26 November 2020, these agreements are for:

- The University of Oxford/AstraZeneca viral vector vaccine, currently in phase 3 trials
- Pfizer/BioNTech mRNA vaccine, currently in phase 3 trials
- Novavax subunit vaccine, currently in phase 3 trials
- The University of Queensland and CSL for their subunit vaccine, currently in a phase I trial

In addition, Australia is a member of the COVAX Facility, a global collaboration to invest in COVID-19 vaccines and make sure they are distributed equitably. The COVAX Facility is jointly led by Gavi, the Coalition for Epidemic Preparedness Innovations (CEPI) and the World Health Organization. There are currently 188 countries, including Australia, participating in the COVAX Facility. Participating countries will have access to a number of vaccines, as and when their safety and effectiveness meet acceptable thresholds through national regulatory authority. Through the COVAX Facility, the Australian Government has made an upfront payment to secure enough doses for up to 50% of the Australian population to be vaccinated.

The government has also made commitments to supporting access to safe and effective COVID-19 vaccines for countries in the Pacific and Southeast Asia.

Q9. When will COVID-19 vaccines be available in Australia?

On the basis of the current progress of the vaccine candidates, the Australian Government anticipates doses of vaccines being made available to people in Australia throughout the course of 2021.

COVID-19 vaccines will be available in Australia after the TGA has assessed extensive data submitted by the vaccine sponsor (company) to demonstrate that a vaccine is safe, effective and manufactured according to appropriate standards.

Supply of the registered vaccine(s) then needs to be secured, which may be through one of the government's Advance Purchase Agreements or through the COVAX Facility.

Finally, the vaccine(s) needs to be manufactured and distributed to immunisation locations.

It has been suggested that vaccine doses could be available as early as March 2020 for those with first priority (refer to Q10), if all of the requirements above are met.

Q10. Who will get a COVID-19 vaccine first and how is this decided?

Even if a safe and effective vaccine is found, it will take time for enough doses to be manufactured so that the entire population can be vaccinated. Initially, the vaccine will need to be offered using a 'priority framework' that outlines how to allocate the initially limited available doses.

The Australian Government, informed by the Australian Technical Advisory Group on Immunisation and other medical experts, will decide which groups to immunise first. Working out the priority groups and the order in which to offer the vaccine will depend on a number of factors that include the distribution of COVID-19 infections and characteristics of available vaccine(s).

As healthcare and aged care workers are at high risk of contracting COVID-19 and also may spread the virus to vulnerable patients and the elderly, they have been identified as one group to be offered the vaccine first. The elderly have also been identified as another priority group. Further information about priority groups is available here.

Children are not an initial priority group for COVID-19 vaccination because of lesser disease severity in children than in older people.

Similar priority lists have been developed around the world, including by the World Health Organization, the United Kingdom Joint Committee on Vaccination and Immunisation and the United States Centers for Disease Control and Prevention.

Q11. Where will people be able to access the vaccine, and will it be free?

Once available, COVID-19 vaccines will be free for all Australian citizens, permanent residents and most visa-holders as per the Australian COVID-19 Vaccination Policy.

As there will be initial limited supplies of the vaccine, priority groups will be offered the vaccines first at vaccination sites. The specific sites used may differ by state and territory, but, for example, are likely to include hospital-based clinics for hospital staff and other workplaces, including aged care facilities.

Once more supplies become available, vaccines will be available through usual immunisation providers, such as general practice clinics, general practice respiratory clinics, for the broader population.

Q12. Will the COVID-19 vaccine be mandatory?

The Australian Government has stated that COVID-19 vaccination "is not mandatory and individuals may choose not to vaccinate". If people choose not to have a COVID-19 vaccine, this will not affect their family's eligibility for Family Tax Benefit Part A or childcare fee assistance which only includes National Immunisation Program vaccines for those aged <20 years.

It is possible that in future, vaccination against COVID-19 might become a requirement for travel to certain destinations or for people working in certain high-risk workplaces. If this becomes the case, there will be exemptions in place for people who are unable to be vaccinated.

Q13. Why are multi-dose vials being used to store COVID-19 vaccines?

Multi-dose vials contain more than one dose of a vaccine in a single glass vial. They usually include 5–20 doses per vial, and each dose is then extracted and given via individual syringes. This is the most efficient way to distribute a new vaccine to the maximum number of people and is being used world-wide for all COVID-19 vaccines.

Packaging vaccine doses multi-dose vials is safe.

Multi-dose vials are routinely used in Australia for the tuberculosis (BCG) vaccine and were used for the 2009 pandemic influenza vaccine. Immunisation providers are trained in and follow guidelines specifically on the use of multi-dose vials when using them.

Q14. What are the likely side effects from COVID-19 vaccines?

All vaccines can cause side effects. Usually these are mild. Early trials of COVID-19 vaccines have reported side effects such as pain at the injection site, fever or muscle aches. All these side effects were temporary.

We will learn more about COVID-19 vaccine side effects as more trial results are published. This FAQ will be updated regularly as more information is available.

Q15. How many doses will be required and what will be the schedule?

The number and timing of doses will vary between different COVID-19 vaccines. Of the vaccines that are currently in phase 3 trials, most require two doses to provide best protection. These doses are usually given 3–4 weeks apart. Only one vaccine that is currently in a phase 3 trial, the Janssen vaccine, is being studied as a single dose.

Q16. What is herd immunity and how does it relate to the COVID-19 vaccination program?

Herd immunity occurs when enough people are vaccinated to prevent the disease easily moving from person to person. Eventually, most of the population may be able to be protected from a particular disease if the vaccine is sufficiently protective and enough people in the population are vaccinated. Achieving herd immunity usually requires a large proportion of the population to be vaccinated. The exact proportion that will need to be vaccinated to affect the spread of the SARS-CoV-2 virus depends on characteristics of the disease (e.g. how easily it is transmitted) and characteristics of the vaccine (e.g. its ability to stop transmission, and duration of protection).

It is easier to generate herd immunity with a vaccine that provides long-term protection and that prevents transmission of the infection between people. Vaccines that provide short-term protection require booster doses, making herd immunity harder to achieve.

As we learn more about the characteristics of COVID-19 vaccines and how well they protect against the disease and spread of the virus, many studies will be done to monitor how much impact the vaccines have and whether herd immunity is being developed over time.

Q17. Will we still need other COVID-19 prevention measures like social distancing and lockdowns if a COVID-19 vaccine is available?

Initially, Australia will still need to have the flexible strategies already in place to control COVID-19. If the vaccine program is effective and starting to reach a high proportion of people, it is hoped that we will be able to reduce some of these control measures. This is likely to be a slow process and will rely on many people being willing to have the vaccine.