Key steps in our journey to a COVID-19 vaccine program

Careful planning is required to deliver a safe and effective COVID-19 program

Providing a safe and effective coronavirus disease 2019 (COVID-19) vaccination program is required to mitigate against the current and future negative impacts on the health and wellbeing of all Australians from COVID-19. An effective vaccination program is a key element required to facilitate economic recovery, safe movement throughout and beyond Australia and a return to the quality of life previously experienced.

Development of COVID-19 vaccines has progressed with incredible speed. Results of phase 3 studies were released in December,[1-3] 11 months after the pandemic was identified. Progress towards a COVID-19 vaccine program has occurred at pace.

Developing a COVID-19 vaccine program

With over 60 candidates in clinical trials, unprecedented efforts are driving vaccine development. Numerous approaches to vaccine design have been utilised, including traditional (inactivated, live attenuated, protein subunit) and more novel approaches (viral vector, nucleic acid).

COVID-19 vaccination program development and registration have progressed in Australia through well established existing pathways and partnerships. The National Immunisation Program was established by the Commonwealth, state and territory governments in 1997 to provide funded vaccines to the Australian population. Partnerships that underpin this program are being used to develop the COVID-19 vaccination program. Vaccines are assessed through the national therapeutics regulator, the Therapeutic Goods Administration (TGA), which assesses safety, quality and efficacy, with advice from an independent body of experts, the Advisory Committee on Vaccines (Box). The Australian Technical Advisory Group on Immunisation (ATAGI) provides technical and clinical advice on the role of vaccines on the National Immunisation Program and oversees development of the Australian Immunisation Handbook. These existing organisations and committees are being utilised for developing the COVID-19 vaccine program.

Funding of vaccines on the National Immunisation Program usually requires submission to the Pharmaceutical Benefits Advisory Committee. If it is deemed cost-effective, the Pharmaceutical Benefit Advisory Committee provides a recommendation to government for funding. Given the need for rapid action, the Australian Government established the COVID-19 Vaccine Taskforce. Potential vaccines are being assessed by government, with advice from the COVID-19 Vaccine and Treatments for Australia – Science and Industry Technical Advisory Group.[4] Ensuring rapid access to COVID-19 vaccines, the Australian Government secured agreements with suppliers of four lead candidates.

A commitment to provide free access to vaccine for all people in Australia has been made.[5]

Leading vaccine candidates

Considering different modes of action and the need for a range of suppliers with international and local manufacturing potential, advanced purchase agreements were signed in 2020 for the University of Oxford–AstraZeneca ChAdOx-1 nCoV-19 (AZD1222) vaccine (a viral vector vaccine); the University of Queensland–CSL V451 and Novavax NCX-CoV2373 vaccines (protein subunit vaccines); and the Pfizer–BioNTech BNT162b2 vaccine (an mRNA vaccine).[6]

Interim phase 3 results have been published for two of these vaccines. Following randomisation of > 43 000 individuals aged ≥ 16 years (predominantly in the United States) receiving two doses of BNT162b2 or placebo, a 95% reduction in symptomatic laboratory-confirmed COVID-19 was reported among vaccine recipients (95% credible interval, 90.3–97.6%).[2] Over 23 000 individuals aged ≥ 18 years were randomised into studies conducted in the United Kingdom, Brazil and South Africa. Randomised individuals received two doses of either AZD1222 (albeit utilising different dosing schedules) or a meningococcal vaccine; a 70.4% (95.8% CI, 54.8–80.6%) reduction in symptomatic laboratory-confirmed COVID-19 was observed.[3] Further results from these trials are anticipated in 2021.

Results from a phase 3 study of NCX-CoV2373 involving more than 15 000 enrolled individuals aged ≥ 18 years were provided (by media release) in January 2021. The first interim analyses reported vaccine efficacy against symptomatic COVID-19 infection of 89.3% (95% CI, 75.2–95.4%).[7]

V451, which uses the human immunodeficiency virus (HIV) gp41 protein to maintain the severe acute respiratory syndrome coronavirus 2 spike protein in its pre-fusion state, generated false positive HIV antibody test results in vaccine recipients in phase I trials. Given potential adverse impacts on the program and the need to modify HIV testing algorithms, further trials of this vaccine were abandoned, with CSL agreeing to increase local manufacturing of AZD1222.[8]

Of the leading contenders, Australia has secured access to 20 million doses of BNT162b2 and 3.8 million doses of internationally manufactured AZD1222, with CSL also committed to locally manufacture 50 million doses of the latter.[7] Much of the global 2021 vaccine manufacturing capacity is tied to pre-market purchasing commitments, with Australia a leader in

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Key steps involved in routine and COVID-19 immunisation programs

	Routine immunisation delivered by the National Immunisation Program	COVID-19 immunisation program
Initiation of process	Sponsor application to the TGA and PBAC	Australian Government with advice from the SITAG
Regulatory decisions	TGA with advice from the ACV	TGA with advice from the ACV
Purchasing decisions	Australian Government with advice from the PBAC	Australian Government with advice from the SITAG
Clinical and other technical information	Statements from ATAGI with support from the NCIRS	Multiple providers, including ATAGI statements, NCIRS fact sheets and training materials contracted by Australian Government Department of Health
Program implementation	Australian Government Department of Health in conjunction with jurisdictions	Australian Government COVID-19 Vaccine Taskforce and Department of Health in conjunction with jurisdictions

ACV = Advisory Committee on Vaccines; ATAGI = Australian Technical Advisory Group on Immunisation; NCIRS = Immunisation Research and Surveillance; PBAC = Pharmaceutical Benefits Advisory Committee; SITAG = COVID-19 Vaccines and Treatments for Australia – Science and Industry Technical Advisory Group; TGA = Therapeutic Goods Administration. ◆

terms of the number of courses available per capita and diversity of vaccines.[9]

In addition, the Australian Government has joined 188 countries in providing funding to the COVID-19 Vaccines Global Access (COVAX) Facility,[10] a key pillar of the World Health Organization (WHO) Access to COVID-19 Tools Accelerator.[11] This enables access to a range of additional candidates but also supports access to vaccines for low to middle income countries.

A critical question is the relative efficacy and real-world effectiveness of current vaccines being trialled. No comparative trials are underway. Despite differences in efficacy point estimates, differences in trial design and study populations preclude any conclusions about their relative impact. For Australians, successful phase 3 studies show that both BNT162b2 and AZD1222 are likely to be effective. Both vaccines are likely to have key roles in the Australian program. Encouraging results from other candidates, including NCX-CoV2373, suggest that these vaccines may also play a role.

Key steps

Essential components of the national COVID-19 vaccine strategy[12] include:

- identifying and supporting research and development;
- building a diverse portfolio of investments and strengthening local manufacturing;
- fostering international partnerships to contribute to the global efforts;
- streamlining regulatory pathways[13] and collaborating with international regulators; and
- working with the ATAGI COVID-19 Working Group[14] to develop a safe and effective vaccination program.

Potential candidates have been reviewed in detail by the TGA and ATAGI, a process which will continue as further data emerge. Provisional determination by the TGA for potential vaccines enables preliminary data to be reviewed ahead of submission of the full regulatory dossier.[13] Full review of lead candidates by the TGA led to approval of both Pfizer–BioNTech BNT162b2 and Oxford–AstraZeneca AZD1222. Ongoing review of other candidates continues.

Advice on priority populations continues to be developed by ATAGI, initially focusing on population groups at greatest risk of exposure, severe outcomes and transmission, in addition to individuals critical to societal functioning such as emergency services, police and public health personnel.[15] Key values (as outlined in the WHO Strategic Advisory Group of Experts on Immunisation values framework) including wellbeing, respect, equity, reciprocity and legitimacy have been considered in identifying priority populations.[16] Prioritisation must be informed by both the epidemiology (with a focus on locations with current community COVID-19 activity) and modelling to examine the impact of varying vaccine characteristics (relative effectiveness, duration of protection) and target populations on overall disease control. Health care and aged care workers have been identified as priority groups for early vaccination in all scenarios.

In addition to sites of routine immunisation delivery, additional locations including dedicated vaccination clinics and workplace and in-reach clinics will be required to ensure timely access for all.[17] Chosen locations will need to consider logistic challenges including storage conditions (the Pfizer–BioNTech vaccine must be stored at – 60°C to – 90°C and used within 5 days of defrosting)[18] and supply in multi-vial trays containing multi-use vials. Workforce development, training and resources (particularly in the safe use of different multi-use vials) are critical components required for a safe and successful program.

Current COVID-19 vaccine trials include 30 000–50 000 participants, of whom roughly half will receive the vaccine. These large studies can detect common adverse events, but to pick up serious but very rare side effects, ongoing monitoring of vaccine safety will be required. Post-marketing surveillance, underway

in the Northern Hemisphere, will provide additional reassurance about the safety of these vaccines. A COVID-19 pharmacovigilance plan, incorporating key vaccine safety programs developed since 2009 including AusVaxSafety (http://www.ausvaxsafety.org.au) and vaccine safety reporting programs established in states and territories, will ensure real-time monitoring of adverse events.

Critical to safety and effectiveness monitoring is use of the Australian Immunisation Register. Amendments to the Australian Immunisation Register legislation requiring mandatory reporting of all vaccines have been passed by Federal Parliament.[19] Additional data systems to streamline reporting to the Australian Immunisation Register and provider education will be required to ensure all administered doses are captured. These changes will ensure all individuals have a valid, durable and reliable record of vaccination. This will assist program rollout (eg, being able to determine which brand a patient has previously received) and also help inform program evaluation (eg, by providing estimates of vaccine coverage at the population level).

Provider and community confidence are paramount to program success.[20] Ongoing research to explore the structural, social and behavioural factors that may compromise vaccine acceptance is required. Clear and regular communication with providers and the public by trusted scientific and public health sources about what is known, as well as uncertainties, is required. The development and dissemination of evidence-based information, along with additional messages for specific target groups and support materials to assist health care providers in discussions with patients, continue to be prepared. A clear and realistic understanding of vaccine effectiveness and expected adverse events are required to combat an anticipated escalation in COVID-19 vaccine misinformation.

As we commence the COVID-19 vaccination program, we enter a new phase of the Australian response to the pandemic. Although millions of influenza vaccines are distributed each year, the COVID-19 immunisation program will be more complex than any other immunisation program in Australia's history. Evidence-informed public policy, collaboration between governments and between program administrators and providers, along with clear communication, are required to ensure programmatic success.

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