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Hot Issue QTB – HUNT

COVID-19 VACCINES AND TREATMENTS

Comparison of COVID-19 vaccines and technology: University of Queensland, Oxford/AstraZeneca, Novavax and Pfizer/BioNTech as at 1 December 2020

Vaccine	Stage and special populations in clinical trials	Technology platform	Clinical trial results	Provisional regulatory status	Manufacturing location/s
University of Queensland/ Seqirus	**Phase 1** trial ongoing in Australia Population groups in trial: 18-55, 56-65 and 66+ years of total 120 participants	Protein + adjuvant	• On 13 November 2020, UQ announced that early data from the Phase 1 trial showed the vaccine was well-tolerated and induced a strong neutralising antibody response, equivalent to or in excess of that in convalescent sera.	• No provisional status available	Australia
University of Oxford/ AstraZeneca	Several large **Phase 3** clinical trials and **Phase 2/3** clinical trials ongoing globally Testing in older adults (>65 years) and individuals with comorbidities (eg HIV)	Adenoviral vector	• On 23 November 2020, Phase 3 trial showed its vaccine candidate had: ○ 90% efficacy in one dosing regimen (half dose followed by full dose), and ○ 64% efficacy in another dosing regimen (two full doses). • An additional trial is planned to fully evaluate the efficacy of the lower dosage regimen.	• Australia: ○ TGA provisional determination* granted 9 October, and ○ TGA has received and is reviewing preliminary data. • International: ○ EU, Canada, UK reviews started	Offshore and Australia

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Novavax	Several large **Phase 2 and Phase 3** clinical trials ongoing globally Testing in older adults (60-84 years) and HIV-positive adults	Protein + adjuvant	• On 22 November 2020, Novavax announced the vaccine prevented infection in rhesus macaques. • Interim analysis from Phase 1 induced neutralising antibody titres exceeded those reported in convalescent sera. • Phase 2 and 3 ongoing.	• Australia: ○ No TGA provisional status available • International: ○ US Fast Track Designation	Czech Republic
Pfizer/ BioNTech	Large **Phase 2/3** clinical trials ongoing globally Testing in older adults (>55 years), younger adults (>16 years) and adolescents (12-18 years)	mRNA	• On 18 November 2020, Pfizer announced Phase 3 primary efficacy analysis demonstrated their vaccine to be 95% effective against COVID-19.	• Australia: ○ TGA provisional determination* granted 14 October, and ○ TGA has received and is reviewing preliminary data. • International: ○ EU, Canada, UK reviews started	US, Belgium

- Provisional Determination allows the TGA to make a decision regarding whether a medicine is eligible for registration via the Provisional approval pathway. Granting of Provisional determination is a prerequisite of the Provisional approval pathway but does not guarantee acceptance of the submission for registration or successful provisional registration on the Australian Register of Therapeutic Goods.

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STANDARD QTB - HUNT

COVID-19 VACCINES AND TREATMENTS

Key points

- The Prime Minister has announced production and supply agreements to secure early access to 134 million doses of a COVID-19 vaccine to Australians in 2021-21 and 2021-22.
- Should these vaccines prove to be successful and safe and meet the Therapeutic Goods Administration's (TGA) stringent assessment requirements and approval processes, Australians will have access to:
    - 33.8 million doses of the University of Oxford/AstraZeneca vaccine, available from early 2021;
    - 51 million doses of the University of Queensland/CSL vaccine, available from mid-2021;
    - 40 million doses of the Novavax protein subunit vaccine, available from the first half of 2021, with the option to purchase an additional 10 million doses in 2022; and
    - 10 million doses of the Pfizer/BioNTech mRNA vaccine, available in the first half of 2021.
- All four vaccine candidates are likely to require two doses per person.
- Novavax's protein subunit vaccine candidate commenced phase three clinical trials in the United Kingdom in September 2020 with up to 15,000 participants (adults).
- The Pfizer/BioNTech vaccine is an mRNA vaccine candidate. It is currently being studied in up to 44,000 participants as part of phase three clinical trials in the United States, Germany, Argentina, Brazil and South Africa.
    - Pfizer has recently applied to the US FDA for Emergency Use Authorisation, which could enable early access to the vaccine without full regulatory approval in the United States. The TGA continues to work closely with international regulators, including the FDA, to collaborate and share information on vaccine regulatory developments.
- The TGA has granted provisional determinations to AstraZeneca Pty Ltd (9 October 2020), Pfizer Australia Pty Ltd (14 October 2020) and Janssen Cilag Pty Ltd (16 November 2020) in relation to their COVID-19 vaccines. This means these companies are now eligible to apply for provisional registration for their vaccines in the Australian Register of Therapeutic Goods (ARTG).
- TGA is unable to confirm whether an application for any COVID-19 vaccine has been received as the current TGA commercial-in-confidence requirements restrict further information being provided on any subsequent application after being granted provisional determination.

- The Australian Government is committed to using local manufacturing as part of its investment decisions. 30 million doses of the University of Oxford/AstraZeneca vaccine and the 51 million doses of the University of Queensland/CSL vaccine will be manufactured onshore with remaining vaccine doses manufactured offshore.
    - CSL has confirmed its Australian manufacturing schedule is on-track to produce 30 million doses of Oxford/AstraZeneca COVID-19 vaccine candidate, and subject to regulatory approvals, first doses would be ready for use early 2021.
- In addition to these advanced purchase agreements, Australia has signed an agreement with Gavi, to join the COVAX Facility for vaccine coverage of up to 50 per cent of Australia's population, approximately 25.5 million vaccine doses.
- On 13 November 2020 National Cabinet endorsed Australia's COVID Vaccination Policy (Vaccination Policy). The Vaccination Policy sets out the roles and responsibilities of the Australian Government and State and Territory Governments in relation to the implementation of a COVID-19 vaccination program in Australia from early 2021.
    - The Australian Government is liaising with the States and Territories to develop jurisdictional COVID-19 vaccination implementation plans.
- On 13 November 2020 the Australian Government published preliminary advice from the Australian Technical Advisory Group on Immunisation (ATAGI) on the priority groups for the first doses of a COVID-19 vaccine. Priority groups identified by ATAGI include:
    - those who are at increased risk of contracting and spreading COVID-19;
    - those who have an increased risk of developing severe disease or outcomes from COVID-19, and
    - those working in services critical to our societal functioning.
- To assist Australians to make informed decisions about receiving a COVID-19 vaccination, the Australian Government and the Department of Health will continue to work closely with state and territory governments, health professionals and expert advisory groups to make evidence-based information readily available.

Recent media

- On 28 November 2020, the UK Government requested the Medicines and Healthcare Products Regulatory Agency (MHRA) (the UK vaccine regulator) assess the latest data and evidence for supply and use of the **Oxford University/AstraZeneca** vaccine under regulation 174 (temporary authorisation/emergency use):
    - On 23 November 2020, Oxford University/AstraZeneca announced results from Phase 2/3 trials of the COVID-19 vaccine candidate (AZD1222). Results reported that across more than 11,000 people the vaccine is highly effective in preventing COVID-19, with one dosage schedule showing a better profile than another. The more effective dosing schedule showed vaccine efficacy of 90% when AZD1222 was given as a half dose, followed by a full dose at least one month apart;

- This method was reported by AstraZeneca on 25 November 2020 as an error during the trial in vial quantity dosage (a mismeasurement of the number of viral vector particles contained within the initial doses), however resulted in a positive efficacy outcome; and

- AstraZeneca announced on 27 November 2020, that an additional trial would be run to evaluate the efficacy of a lower dosage regimen that was found to have performed better than the full amount in AstraZeneca studies. This is due to the high efficacy in lower dosing regimen that warrant further assessment to establish the most effective regimen for evaluation and regulatory submission.

- On 20 November 2020, the **Australian National University** released results from a study of 3000 Australian participants examining how demographic, attitudinal, political and social attitudes and COVID-19 health behaviour correlates with vaccine hesitancy and resistance to a COVID-19 vaccine. When asked if a safe and effective vaccine for COVID-19 is developed almost 3 in 5 Australians (58.5 per cent) would definitely get the vaccine, 28.7 per cent were likely to get a vaccine, 7.2 per cent unlikely and 5.5 per cent resistant.
- On 17 November 2020, **Moderna** announced that interim (unpublished) Phase 3 data suggested their vaccine may be 94.5 per cent effective in preventing COVID-19 in participants.
- On 16 November 2020, TGA granted a provisional determination to **Janssen-Cilag Pty Ltd (Johnson & Johnson)** in relation to its COVID-19 Vaccine, Ad26.COV2.S. The granting of a provisional determination means that the Therapeutic Goods Administration has made a decision that Janssen is now eligible to apply for provisional registration for the vaccine in the Australian Register of Therapeutic Goods.
- On 13 November 2020, the **University of Queensland** announced that early data from the Phase 1 trial showed the vaccine was well-tolerated and induced a strong neutralising antibody response.
- On 9 November 2020 **Pfizer** announced that preliminary Phase 3 data suggests their COVID-19 vaccine may be 90 per cent effective in preventing COVID-19 in participants. On 11 November 2020, it was noted that the Australian Government is currently working closely with the pharmaceutical manufacturer, Pfizer, Australian logistic experts and the State and Territory Governments on storage and handling arrangements to support the rollout of the Pfizer mRNA vaccine.

Facts & figures

Clinical trials

- As at 12 November 2020, there are **more than 212** vaccine candidates in **pre-clinical** and clinical trials, including **48** undergoing **clinical trials in humans**.

- **Ten candidates have entered Phase III trials**, including candidates from the University of Oxford/AstraZeneca, Pfizer/BioNTech, Janssen, Novavax and Moderna.

- **Six vaccine candidates have commenced clinical trials in Australia**. This includes candidates developed by the University of Queensland, Flinders University/Vaxine, Novavax and four being developed by international companies; Novavax and Clover Biopharmaceuticals (both with support from CEPI), Symvivo and SpyBiotech/Serum Institute of India/Accelagen.

- As of 26 October 2020, there are over 1,970 COVID-19 clinical trials evaluating treatments globally.

Funding

- Over $3.8 billion has been allocated for the first tranche of investments to support the development and production of a safe and effective vaccine in sufficient quantities to ensure all Australians have early access when it becomes available. Investments include:

    - $1.5 billion, announced by the Prime Minister on 5 November 2020 for two new COVID-19 agreements for the supply of promising COVID-19 vaccines, between the Australian Government and Novavax Inc. and Pfizer/BioNTech;

    - $123.2 million announced on 21 September 2020, as an initial commitment to formally join the COVAX Facility. This will provide vaccine coverage of up to 50 per cent of Australia's population, with purchases of vaccine doses being negotiated on a case-by-case basis as testing data becomes available;

    - $1.7 billion, announced by the Prime Minister on 7 September 2020 for production and supply agreements with the University of Oxford/AstraZeneca (Oxford) and the University of Queensland/CSL (UQ) COVID-19 vaccines, securing early access to approximately 84.8 million vaccine doses in 2020-21 and 2021-22;

    - $24.7 million, announced on 19 August 2020 for the purchase of peripherals to enable COVID-19 vaccine administration from Becton Dickinson;

    - $80 million to secure COVID-19 vaccines for developing countries through the Advance Market Commitment component of the Gavi Facility.

    - $367 million on research investment for diagnostics, vaccine development, antiviral development, clinical trials, digital health research infrastructure and research into the human immune response to COVID-19 infection. This comprises:

        - Over $96 million through the Medical Research Future Fund for research into COVID-19 related vaccines and treatments, as well as further preparedness;

        - $2 million to APPRISE (the Australian Partnership for Preparedness Research on Infectious Disease Emergencies);

        - $20 million to an Australian Defence Force anti-viral (chloroquine) trial;

- $15 million to Coalition of Epidemic Preparedness Innovations (CEPI) and the Foundation for Innovative New Diagnostics (FIND);
- $230 million investment in the CSIRO's vaccine development capability; and
- $3.5 million of a total $11.7 million investment (with Brandon Capital Partners) from the Biomedical Translation Fund to develop an innovative nasal treatment.

Response/If asked

Are there any plans to purchase the Moderna vaccine?

- The Australian Government is closely monitoring vaccine development and progress of clinical trials around the world, and is pleased to see the progress of the Moderna. candidate.
- Australia may be able to access the Moderna vaccine, should we require it, through the COVAX Facility.

Prioritisation

- The Australian Government recognises the global imperative to find a safe and effective vaccine to end the COVID-19 pandemic. Due to this demand, it is likely large volumes of doses will not be immediately available but prioritised month-to-month. This is why we need to prioritise which groups have access to the vaccine first.
- Decisions on the implementation of a vaccination program, if and when a vaccine becomes available, are being informed by a number of experts including the Australian Technical Advisory Group on Immunisation (ATAGI).
- On 13 November 2020 the Australian Government published preliminary advice from ATAGI on the priority groups for the first doses of a COVID-19 vaccine. This preliminary advice is consistent with guidance from the World Health Organization (WHO).
- The three priority groups identified to date by ATAGI are:
    - Those who are at increased risk of exposure and hence being infected with and transmitting SARS-CoV-2 to others at risk of severe disease or are in a setting with high transmission potential;
    - Those who have an increased risk, relative to others, of developing severe disease or outcomes from COVID-19; and
    - Those working in services critical to societal functioning.
- As further data become available, this advice will be updated to develop priority groups for each vaccine.

Locations of vaccination

- Key vaccination sites are include GPs, GP Respiratory Clinics, state and territory vaccination sites and some key workplaces (such as residential aged care where appropriate). This is being discussed with States and Territories.
- The Australian Government will be working closely with States and Territories to ensure the vaccination sites can facilitate a COVID-19 vaccine program. This will be further outlined in the individual State and Territory implementation plans which are currently being developed between the Australian Government and State and Territory Governments.

Logistics and data arrangements or procurements

- The roll-out of a potential COVID-19 vaccine is a significant challenge of logistics and will require strong partnerships with specialists who can safely handle and track the vaccine doses.
- There is a huge amount of work being done to make sure Australia is ready for a COVID-19 vaccine and it is critical that we continue to do this at a rapid pace so we can take this important step towards the end of the pandemic.
- This will involve:
    - storing and moving vaccine doses at the appropriate temperature, which for some vaccine types can be well below freezing;
    - tracking the location of vaccine stock at any time;
    - This involves the integrating data from many existing systems and sources so that there is a central source of information about each dose and each vial; and
    - protection of the physical security of doses and cyber security of information at all times.
- The Department is currently assessing proposals via limited tender for:
    - an end-to-end solution for vaccine storage, distribution and logistics; and
    - a data consolidator providing end-to-end visibility of the COVID-19 vaccine.

Cold chain storage

- The Government has secured purchase agreements with a range of promising vaccine candidates to give Australia the best chance of receiving safe and effective vaccines.
- Different vaccines may have different temperature storage needs.
- We are preparing for three temperature requirement scenarios: 2-8 ºC, -20ºC and -70ºC

- This range of cold chain storage options covers all of the vaccine candidates likely to be considered for use in Australia.

- An mRNA vaccine requires ultra-cold storage and transportation.
  The Australian Government is working closely with the pharmaceutical manufacturer, Pfizer, Australian logistics experts and the State and Territory Governments on storage and handling arrangements to support the rollout of Pfizer's vaccine.

Concerns over the number of vaccines procured

- The Australian Government is committed to providing all Australians with access to safe and effective COVID-19 vaccines as soon as available and is pursuing a diversified portfolio of vaccines, ensuring that Australia is well placed to access a successful vaccine.

- All vaccine candidates are expected to require two doses. While the Australian Government is optimistic that the Oxford, UQ, Novavax and Pfizer/BioNTech vaccines will result in safe, effective vaccines, this is new science and only comprehensive data from Phase 3 trials will be able to confirm this. It is possible that one, or more, of these vaccines will be unsuccessful.

- The vaccine agreements also allow us to support our Pacific and South East Asian neighbours, as all vaccine agreements allow us to donate or on sell (with no mark-up) vaccine doses to other countries or international organisations.

Mandatory/Compulsory Vaccination

- The Australian Government is a strong supporter of immunisation that it is a safe and effective way to prevent the spread of many diseases in the community that can cause hospitalisation, serious ongoing health conditions, or even death.

- While the Government supports immunisation, it is not mandatory and individuals maintain the option to choose not to vaccinate.

- The vaccine will be available for free to those who choose to be vaccinated.

- It is important that everyone who can benefit from a COVID-19 vaccine, can access it to protect themselves, their loved ones and their community.

- Any decisions regarding the availability of a potential COVID-19 vaccine and related policies will be based on the advice of the Australian Technical Advisory Group on Immunisation and other experts, and will be contingent on a vaccine candidate meeting all requirements with regard to testing and safety.

- A COVID-19 vaccine is the best way to protect the Australian community.

Vaccine safety

- The TGA rigorously assesses vaccines for safety, quality and effectiveness, before they can be legally supplied in Australia. These are strict requirements, because vaccines are routinely given to healthy people in large numbers.

- The TGA is actively monitoring COVID-19 vaccine development that is occurring both in Australia and around the world and is meeting with pharmaceutical companies to discuss progress and the application process.

- The Department of Health is monitoring the progress of vaccine candidate clinical trials; including the occurrence of any adverse events.

    - The Department is aware of the pauses to the trials of the Oxford/AstraZeneca and Johnson & Johnson (Janssen) vaccines.

- Phase 3 trials are undertaken to study the efficacy and safety within large groups of people (tens of thousands), and to determine potentially rare side effects. It is not unusual to pause a clinical trial to investigate adverse events. The voluntary pause on this clinical trial demonstrates the commitment to ensuring a safe and effective product and that the appropriate regulatory reviews are being undertaken to identify and manage challenges.

- When evaluating an application to register a vaccine, the TGA carefully assesses safety data including adverse events that may have been responsible for a clinical trial pause.

- The TGA is also part of a network of international regulators that meet regularly to discuss the development of COVID-19 vaccines.

- This information, together with the potential to use already established work-sharing arrangements and collaboration with other international regulators, will assist the TGA to expedite the evaluation of any new vaccines without compromising on strict standards of safety, quality and effectiveness.

- Once registered, a COVID-19 vaccine will continue to be closely examined after introduction via additional clinical trials, surveillance and monitoring of adverse events.

Treatments

- Several treatments are currently available for use in Australia, for example provisional approval has been granted by the TGA to use remdesivir in hospitalised COVID-19 patients with severe disease.

- The Australian Government is closely monitoring treatments in clinical trials and will take appropriate action as required.

- In Australia, the National COVID-19 Clinical Evidence Taskforce (the Taskforce) prepares and revises weekly high-priority, evidence-based clinical guidelines which include recommendations for disease-modifying treatments.
    - The Taskforce currently makes recommendations for the use of remdesivir and dexamethasone in specific patient populations with specific severity of COVID-19; and
    - The Taskforce currently does not recommend the use of hydroxychloroquine or lopinavir/ritonavir for COVID-19 patients outside of randomised trials with appropriate ethical approval.
- Regeneron has four clinical trials registered to evaluate REGN-COV2, an infusion of two monoclonal antibodies that target the spike protein of SARS-CoV2.
- On 4 October 2020 it was reported US President Donald Trump was receiving three experimental treatments for COVID-19: with remdesivir (an antiviral), dexamethasone (a steroid), and the Regeneron (an antibody infusion) treatment REGN-COV2.
    - Each of these treatments are a part of ongoing clinical trials for use in COVID-19; and
    - Australian Nobel Prize-winning immunologist Professor Peter Doherty said in an address to the Melbourne Press Club on 5 October 2020, “We're hoping these are going to work really well on President Trump ... because that's our best shot out there at the moment for a specific therapy”.

Global efforts

- Australia is working internationally to forge bilateral and multilateral partnerships to support not only Australia but the world, including the Indo-Pacific, to access an effective COVID-19 vaccine.
- Australia is committed to ensuring affordable and equitable access to effective COVID-19 vaccines, treatments and diagnostics once they become available.
    - The May 2020 World Health Assembly resolution on the COVID-19 Response, co-sponsored by a record-breaking 145 countries including Australia, acknowledges the critical need for equitable and affordable access to quality, efficacious medical products, medicines, and vaccines;
    - Australia strongly support international efforts under the multilateral Access to COVID-19 Tools Accelerator (ACT Accelerator) process to develop, manufacture and fairly allocate these urgently needed tools; and

- Australia also supports WHO's efforts to develop a Global Framework to ensure Equitable and Fair Allocation of COVID-19 Products and is engaging closely in the development of this Framework.

- On 31 October 2020, the Foreign Minister announced Australian support for COVID-19 vaccine access in the Pacific and Southeast Asia.

    - The Australian Government will provide a range of support including supplying safe and effective vaccine doses and delivering technical support to our regional partners. Australia will assist with assessment of vaccine safety, efficacy and quality by national regulatory authorities, informed by WHO advice;

    - An additional $500 million has been committed over three years towards this effort on top of the $23.2 million committed in the Budget; and

    - The funding will further help ensure that the countries of the Pacific and Timor-Leste are able to achieve full immunisation coverage, and will make a significant contribution toward meeting the needs of Southeast Asia.

COVAX Facility

- On 21 September 2020, Australia signed an agreement with Gavi, the Vaccine Alliance to formally join the COVAX Facility. The agreement provides the option to purchase successful COVID-19 vaccines from a broad portfolio of candidates to cover up to 50 per cent of Australia's population.

- The Facility is an important component of Australia's COVID-19 Vaccine and Treatment Strategy and serves as insurance for our Advanced Purchase Agreements in the event they do not meet our domestic needs.

- A total of 156 countries have committed or are eligible to receive vaccines through the Facility, which represents the best multilateral effort to end the acute phase of the pandemic in both developed and developing countries.

- The Australian Government announced an investment of $80 million in the COVAX Advance Market Commitment (AMC) to benefit the region.

    - This contribution, announced by the Foreign Minister on 24 August 2020, equates to sufficient COVID-19 vaccine doses to meet the needs of the highest risk populations in the Pacific and Timor-Leste, as well as a contribution to Southeast Asian needs.

- The CEPI/Gavi-led COVAX Facility aims to pool global resources to accelerate the development and distribution of COVID-19 vaccines.

Liability

- Given the unprecedented pandemic circumstances, vaccine development is being accelerated, however, all vaccines are still required to meet stringent safety and efficacy guidelines. For any vaccine to be registered, it will have been assessed by the Therapeutic Goods Administration for safety and effectiveness, and where appropriate informed by experts on the Australian Technical Advisory Group on Immunisation. Once registered, a COVID-19 vaccine will continue to be closely examined after introduction via additional clinical trials, surveillance and monitoring of adverse events.

- The Government has acknowledged the need to appropriately share risks associated with achieving early access to a successful vaccine, and has actively engaged with potential COVID-19 vaccine suppliers on this issue.

- As noted in the 2020-2021 Budget papers, through the relevant Advanced Purchasing Agreements (APAs), the Australian Government has subsequently provided an indemnity to the suppliers of the University of Oxford vaccine candidate, which is sponsored by AstraZeneca, and the University of Queensland vaccine candidate, which is marketed by Seqirus, covering certain liabilities that could result from the use of the vaccine.

- Specific details contained in the APAs, including those around indemnity are not public and the Australian Government is conscious of maintaining commercial confidentiality of the arrangements.

- The effect of the indemnities is that the Australian Government agrees to be liable for claims by individuals as a result of the use of the vaccines, subject to the terms of the relevant agreement.

- The Government is not pursuing a no-fault COVID-19 vaccine injury compensation scheme at this time.

Communications strategy

- The Department of Health will be a source of timely, fact-based information. A dedicated section on the Department's website is already available for people to view such information.

- External sources of reputable information on vaccination in Australia are also available on the Department's website.

- We know that our health sector will play an important role in delivering such information to Australians. Health professionals are a trusted source of information, and will be vital in getting our messages out there.

- The Australian, state and territory government will continue to engage with the sector so our health professionals are well equip to assist their patients in accessing COVID-19 vaccine information, and empower them to make decisions about vaccination.

MO COMMENTS [MO input only]

Contact Officer: Assistant Secretary	Nick Henderson	Work Phone: (02) 6289 3917	Mobile Phone: s 22
Cleared by: First Assistant Secretary	Lisa Schofield	Work Phone: (02) 6289 7480	Mobile Phone: s 22