Australian Government
Department of Health
Therapeutic Goods Administration

Pharmacy Guild update
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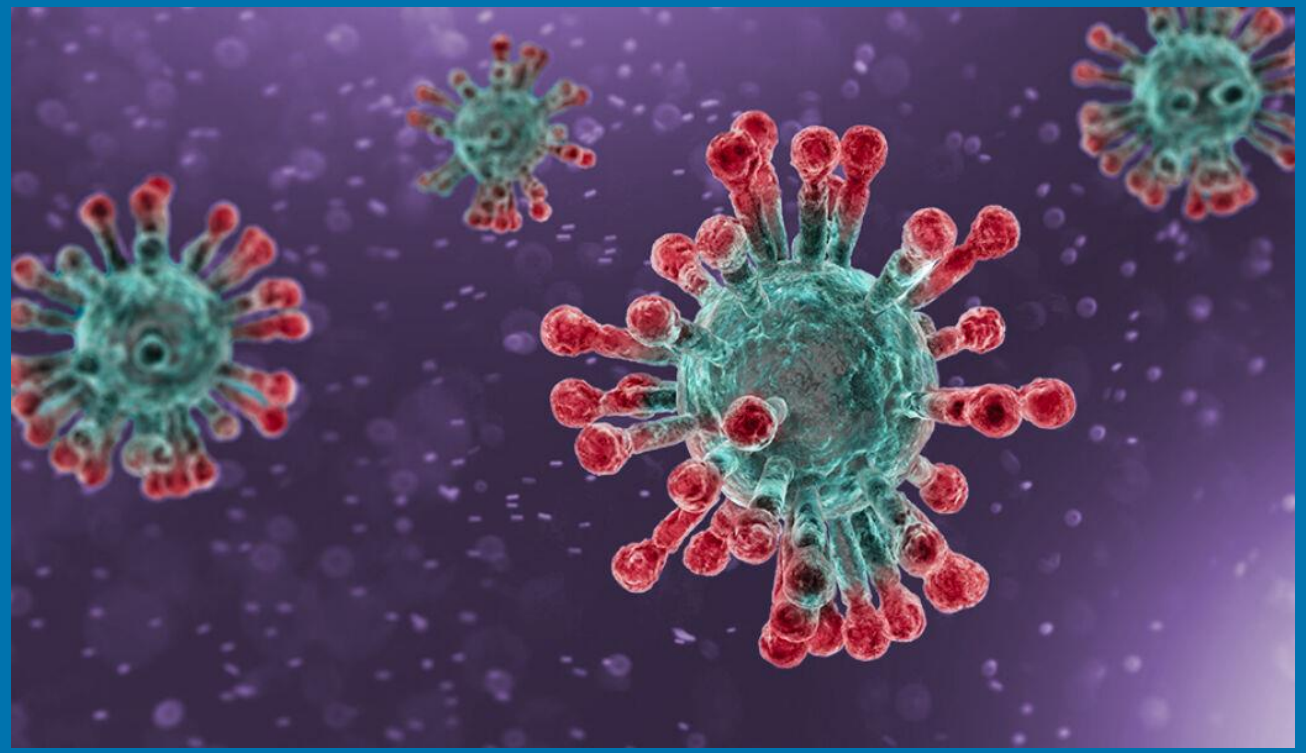
TGA Health Safety Regulation

COVID-19 vaccines, therapeutics and rapid antigen tests



What data does TGA review ?

Efficacy

- Types and level of immune responses induced by the vaccine
- Clinical trials - vaccine must very significantly reduce COVID-19 in large numbers of subjects vs controls

Quality

- Manufacture at each site according to international standards of GMP and consistency
- Purity of the vaccine components and its potency and stability
- Batches and documentation evaluation by TGA labs before supply

Safety

- Toxicology data from experimental animals
- All side effects need to be reported in the regulatory submission
- Participants in clinical trials must be followed post trials, also real world data

How were the vaccines approved so quickly?

Pfizer (54), AstraZeneca (48), Janssen (136), Moderna (23 working days)

We have been criticised both for being too slow and too fast !

- **Preliminary discussions with sponsors** months before the submissions lodged
- **Rolling submission of data –** data reviewed by TGA as soon as it was available
- **Collaboration with international regulators**
- **Teams worked in parallel and staff worked long hours** and weekends
- **Advisory committee** meetings with 2-3 days (rather than with 2 weeks) notice
- **Sponsors' response to questions** expedited
- Provisional approval means that **some data will be provided after registration**

What further vaccines are coming along ?

Approved or being considered overseas – we will consider soon

- Third vaccination for the **immunocompromised**
- **Booster shots** – for those 6-12 months
  - Pfizer – FDA approval – elderly, healthcare and front line workers – 17 Sep 21
  - Moderna and Janssen – FDA advisory committee 14-15 Oct 21
  - UK approval for booster, EMA decision soon
- **Pfizer for 5-11 year olds** – FDA advisory committee 26 Oct 21
- Novavax – quality and manufacturing data may not be submitted until November

We will get more applications in 2022

- Vaccines against variants ?
- Applications for 6 month to 5 years olds
- Other candidates – new mRNA/DNA/ other technologies, overseas vaccines

COVID-19 Vaccine Pharmacovigilance

Monitor Vaccine Safety

- **Common reactions** - fever, chills, pain, fatigue, headache
- **Serious adverse events of "special interest"** undergo intensive monitoring and investigation
- **Information comes from reports from GPs, public, industry**
- **How are the signals analysed ?**
  - By event type, patient age, location, batch number
  - Comparing observed vs expected "background" rates
  - Causality is key - expert panel reviews new serious events
- **Transparency supports public confidence** but data can be used by some to mislead or alarm
- TGA will also have a central role in the **Government's vaccine compensation scheme**

Pfizer (Comirnaty) vaccine and myocarditis

115 likely cases of myocarditis, also reports of pericarditis (30 September)

- Myocarditis rate 7 per million overall - but 47 per million in second dose under 20s
- Rates higher for second dose in younger males, most cases not serious
- Myocarditis also much more common in COVID-19 infected people than in vaccinated people
- Moderna – no Australian data – debate as to whether myocarditis rates are higher than for Pfizer
- Pharmacists should encourage people with chest pain, palpitations, fainting or shortness of breath to seek medical attention, especially if 1-5 days post vaccination
  - Testing includes ECG, chest X-ray and troponin
  - Defer second doses of Pfizer or Moderna if myocarditis or pericarditis happens after dose 1

Other AESI being monitored

- Anaphylaxis (very rare), multisystem inflammatory syndrome (not confirmed)

AstraZeneca (Vaxzevria) vaccine adverse events

Thrombosis with thrombocytopenia

- Rare syndrome – 148 cases from 11.6 m doses
- Not a significant age/gender difference, but more serious cases in younger women
- 8 deaths – less than 1 in a million rate
- 16 cases after second dose – all in over 50s, most less serious

Guillain Barre Syndrome (immune disorder affecting nervous system) – 129 reports

- clear link not established but warning added to Product Information

Immune Thrombocytopenia – 75 reports

- One fatal case likely vaccine related but others not definitively linked

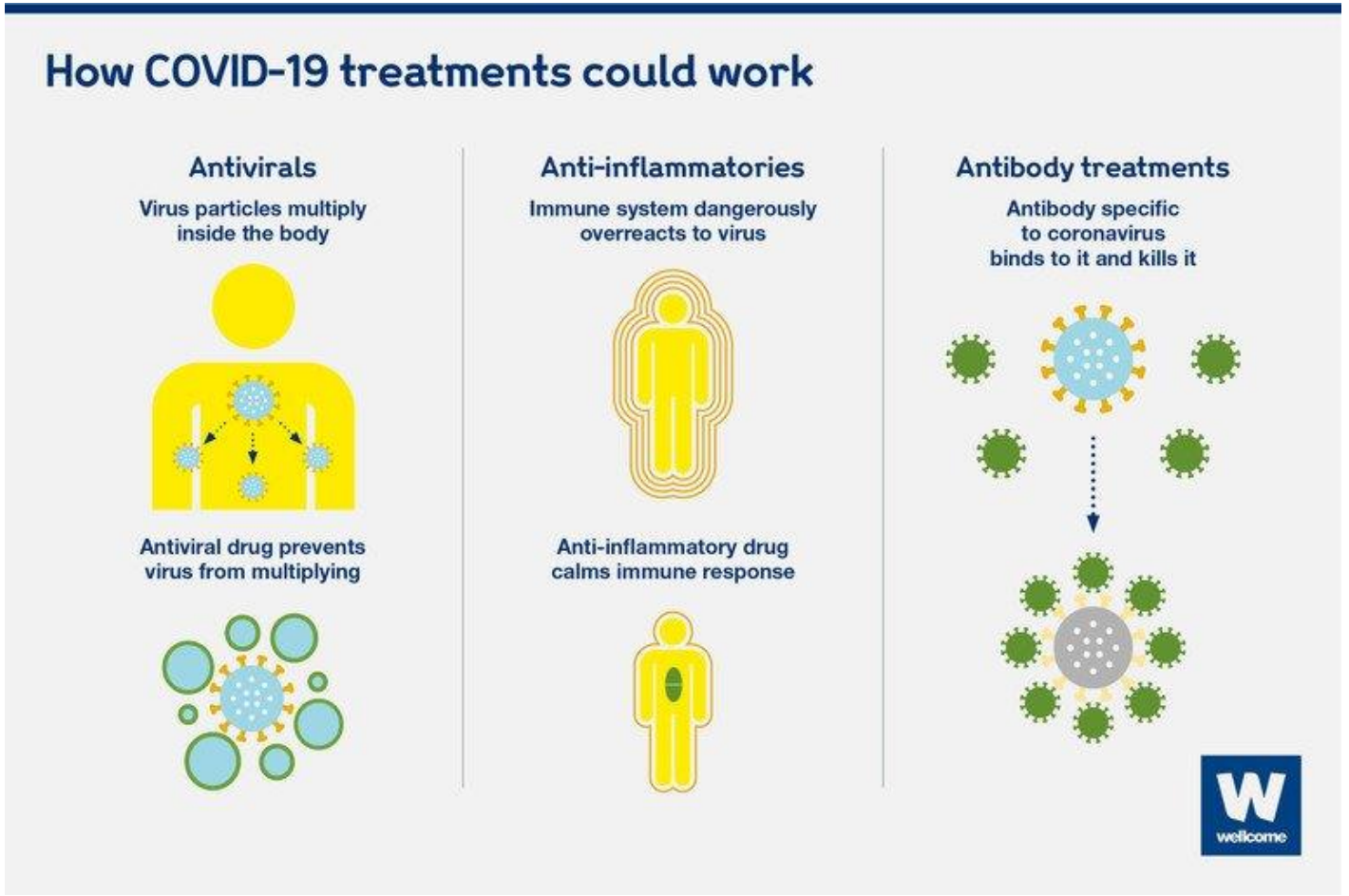
Other reports (both vaccines) but causality not confirmed

- Bell's palsy, skin reactions, menstrual disorders, multisystem inflammatory syndrome

COVID-19 treatments

Being developed and used for different scenarios

- **Treatment of late stages of COVID-19** – reduction of deaths in ventilated patients
- **Prevention of disease progression** in high risk patients (hard to identify most suitable individuals)
- **Prophylaxis** (including pre- and post exposure)



Therapeutics for COVID-19 infections

- **Five main medicines currently in use in Australia**
  - **Corticosteroids** (patients on oxygen) – **off label use**
  - **Remdesivir** (moderate to severe COVID-19 in patients not requiring ventilation) – **TGA approved**
  - **Sotrovimab** (patients at risk for progression to hospitalisation or death) – **TGA approved**
  - **Tocilizumab** (patients on oxygen, and with inflammation) – **TGA provisional designation**
  - **Baricitinib** (JAK inhibitor for patients requiring oxygen) - **off label use**
- None yet for outpatient/community use
- No ‘magic bullet’ antivirals for COVID-19 - such as for Hep C or HIV/AIDS

Treatments with provisional designation by the TGA

(but the companies still have to submit their data for evaluation)

Antiviral monoclonal antibodies – intravenous/intramuscular

- REGNCoV2 **Casirivimab/Imdevimab (Roche)** – prevention of disease progression, prophylaxis ?
- **Regdanvimab (Celltrion)** – iv administration – prevention of disease progression

Oral antiviral may find wider community use but are a few months away

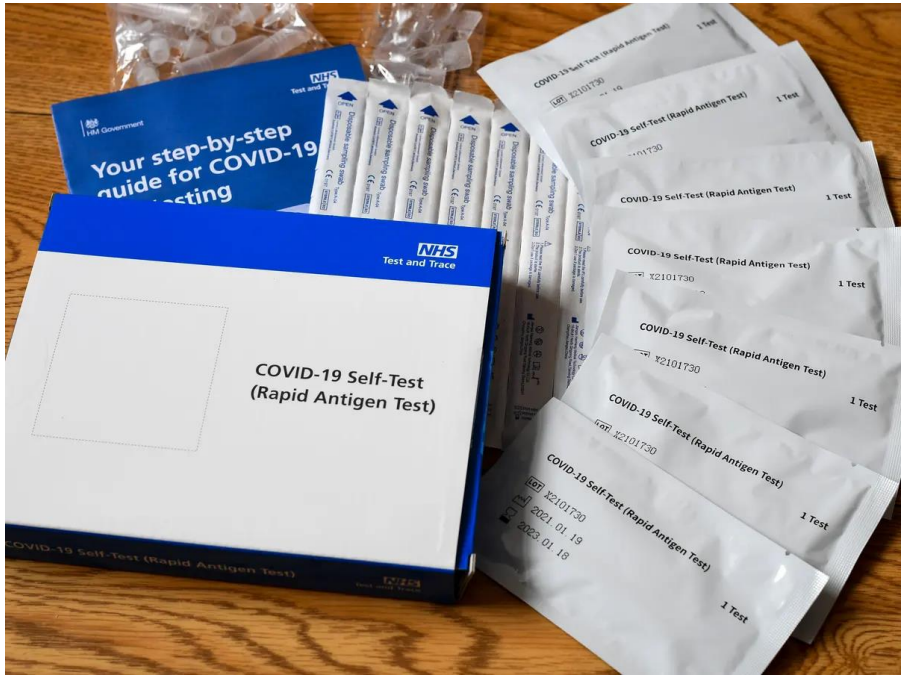
- **Molnupiravir (MSD)**
  - Inhibits viral replication, preventing progression of mild-moderate disease
  - Interim phase 3 trials – 7 % treated and 14 % placebo hospitalised (and 0 vs 8/ 775 died)
- **PF - 07321332 plus ritonavir (Pfizer)**
  - Viral protease inhibitor (while ritonavir slows its metabolism)
  - Prevention of disease progression plus use in post exposure prophylaxis

Rapid antigen tests – current situation

- **Already reasonably widely used** in health care/ aged care facilities, construction, logistics, customer service businesses
- **Sampling/ testing must be supervised by a trained person** but a healthcare professional does not need to be present
- **Useful screening tool** but will miss cases early and late in infection
- Kits currently on Australian market **designed for professional oversight but not self-use**

What about overseas self test kits ?

- Many **developed prior to delta strain becoming predominant**
- Use in **countries with much higher COVID-19 prevalence** doesn't automatically translate to Australia e.g. average daily cases last week
  - Australia 1849, UK 34254, USA 108139
  - Contact tracing remains important in Australia
- The **TGA approved self tests** will pass performance, useability testing and have Australian contact details



What modifications are needed for self testing ?

- **Simpler instructions for use**
- **Usability testing** with untrained users
- Contact centre for users (1800 number, interactive website)
- Confirm they detect the **delta** variant well – independent evaluation
- TGA regulation to enable **responsible advertising**
- Mandate **reporting of problems -** false positives and negatives

An evolving situation

- Early September – TGA invited companies to submit expressions of interest and early data
- October 1 – sponsors can submit formal applications to TGA
- November 1 – tests will be able to be available online or from pharmacies or any retail outlet

Trusted community pharmacists have an important role to play !!!