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Position Paper - National Testing Strategy for COVID-19 Recovery

Pathology Technology Australia is the peak body representing the manufacturers and suppliers of pathology testing products used in pathology laboratories, hospitals, in community clinics and for home testing. As such we are the only entity in Australia to hold an integrated picture of the installed base of pathology testing platforms, including the total throughput and capacity of these systems. In addition, we hold the knowledge of test availability for existing and new technology. We also have clear sight of test development and supply for COVID-19 now and into the future.

There is likely to be a massive global demand for high quality COVID serology tests. This highlights the importance of Australia rapidly agreeing on and communicating a National Testing Strategy for COVID-19 Recovery.

By partnering with healthcare professionals, pathology technology companies and both public and private pathology services, this Strategy can be fully committed to and successfully executed.

Executive Summary

- With promising signs that COVID-19 infections in Australia are slowing, a "back to it" strategy can be implemented.
- Pathology Technology Australia proposes a standardised, National Testing Strategy for COVID-19 Recovery, to guide implementation and to ensure health services are presented with a manageable COVID-19 caseload.
- The National Testing Strategy will consist of a combination of existing Nucleic Acid Testing (NAT) for viral RNA and high-quality serology tests for COVID-19 antibodies and antigens.
- The National Testing Strategy needs to be endorsed and signed off by the Commonwealth and agreed to by all State and Territory governments, possibly through the National Cabinet.
- State governments should acquire the tests and execute the strategy in public pathology labs and private pathology labs should have an MBS reimbursement item to support execution in their facilities.
- This National Testing Strategy will allow people and businesses to resume their livelihoods, reducing the burden on government spending to sustain the economy.
- Testing will be offered in tailored recommendations for specific population groups.

- For a quick response to scale-up testing, the main testing burden for NAT and serology should be conducted in the existing infrastructure of public and private laboratories. Point of care testing will be required in specific settings, such as regional and remote locations, and as required for better patient management.
- NAT point of care testing is an emerging segment and the range of technology choices released to the market will increase over time. Consideration needs to be given to ensuring facilitated, end-user access to a broad range of point of care technology options. This will enhance the delivery of robust and reliable point of care results for COVID-19 and other time critical tests.
- All testing technology for NAT and serology (including lateral flow antibody tests and point of care) will need to meet quickly determined agreed upon minimum performance characteristics and data transmission requirements prior to implementation.
- Until a vaccine or effective treatments are available, there will need to be a strategy devised to protect vulnerable members of society.
- Technology assessment services such as those offered at the Doherty Institute (for NAT products) and the NRL (for serology products), should be used where test performance characteristics require validation.
- Automated data collection and transmission for all COVID-19 testing and the COVID infection tracking app will be critical parts of this strategy. Consider integrating diagnostics data and the tracking app should privacy requirements permit.
- New MBS reimbursements will be necessary for serology and point of care testing, to ensure the strategy is executed fully and in all parts of Australia.

Objectives of the National Testing Strategy for COVID-19 Recovery

Establish, fund and execute a standardised, national testing protocol – that is rolled out across Australia, through the existing accredited pathology infrastructure and community healthcare professionals.

- Enabling safe return of people to their workplaces and to a reasonable level of social interaction.
- Protecting the vulnerable.
- Maintaining COVID-19 related hospitalisation, ICU admissions and ventilator requirements to less than 20% of all-cause admissions.
- In conjunction with a suitable tracking and tracing system, provide data on new infections, personal and population immunity, and to guide re-institution of social measures if necessary.

Facilitating testing capabilities to meet these objectives, pathology technology manufacturers (both globally and in Australia) have compressed years of test development and validation into months, thus providing high quality diagnostics testing for COVID-19.
Manufacturing capacity has been scaled significantly by leveraging proven capabilities and quality processes. The traditional manufacturers across the USA, Europe and the Asia Pacific region are now ramping up production to between 5 and 10 times their former quantities. These suppliers have the highest quality and manufacturing processes, recognised by the TGA and the major accrediting bodies around the world. In addition, stringent post market surveillance ensures testing remains safe and efficacious.

Recommendations - National Testing Strategy for COVID-19 Recovery

- It is our recommendation that a combination of NAT and serology testing be adopted as front-line testing for the Australian population. We recommend a strategy for initial viral NAT and Serology testing for antigen and antibodies, in simultaneous collections of nose/throat swab and venepuncture blood test.
- This strategy provides the highest possible diagnostic accuracy and provides baseline data for future comparison.
- In addition, we recommend a testing protocol for specific groups of people, depending on occupation or risk of exposure. Depending on the group, these may require only serology tests.
- We recommend most of this testing be performed in accredited pathology laboratories using the established infrastructure for testing and sample collection.
- We also recommend establishment of a distributed point of care testing network infrastructure, where healthcare professionals can provide NAT and serology tests in regional, remote and time critical settings and where urgent patient management decisions need to be made. This will require a change to current testing strategies and funding but will provide far greater flexibility for managing existing and future health challenges.
- Our recommendation facilitates a rapid roll out and execution. It also facilitates high levels of COVID-19 data collection which will provide real-time input for tracking and tracing and to study immunity patterns.
- Our capability audit of the sector indicates there is enough capacity in the existing infrastructure for sample collection and testing, without adversely impacting other healthcare testing.

- Our recommendation is for the Commonwealth and States, via the National Cabinet, to agree on a National Testing Strategy for COVID-19 Recovery and communicate this widely.
- We recommend execution of the Strategy through the public and private pathology infrastructure
- Funding for the Strategy be facilitated through grants to the states and territories and through MBS item numbers for both point of care and testing in private pathology labs.

Current COVID-19 Transmission in Australia

As of 21st April, there were 6640 confirmed cases of COVID-19 infection in Australia and 71 deaths, with the rate of new infections decreasing as a result of a combination of quarantine, isolation, social distancing and hygiene measures. At the time or writing, 170 people across Australia are hospitalised (7% of current cases), 49 (2%) of these in ICU and 32 (1%) require ventilation.

The source of infection has been determined as follows:

- The majority (64%) of the COVID-19 infected individuals contracted the infection whilst overseas.
- The next most common source of infection is locally acquired from contact with a confirmed case (24.8%). This is expected to be the most common source of new infection moving forward.

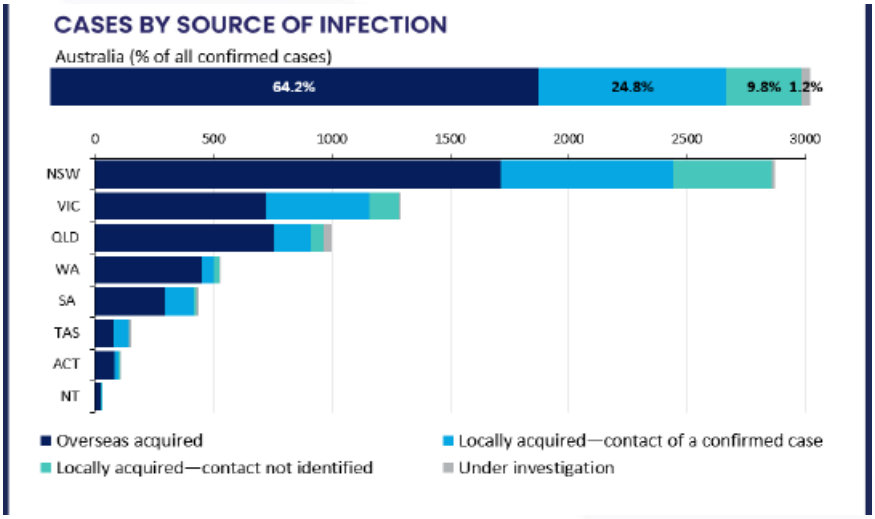

Table 1. Covid-19-cases-in-Australia-by-state-and-source-of-transmission[5]

Since the commencement of NAT for SARS-CoV-2 to aid diagnosis efforts, more than 420,000 tests have been conducted. 1.6% of tests have been positive.

Recent recommendations by the Communicable Diseases Network Australia should lead to testing a broader cohort of Australians potentially exposed to the virus which could help identify viral presence in the community more actively and assist in implementation of population serology testing.

Manufacturers are increasing production to maintain a high-level capacity for SARS-CoV-2 NAT, not only the supply of manufactured NAT kits but also the probes and primers required for lab-developed tests. This will be important as the government looks to release some containment measures and manage potential future outbreaks. Current initiatives, including appropriate MBS reimbursement for COVID-19 molecular tests are enabling both private and public laboratories to support the diagnostic testing demands, notwithstanding that supply is still a challenge for both tests and associated consumables. Continued support from both federal and state governments needs to be maintained to ensure Australia is one of the most successful countries to deal with the COVID-19 pandemic; which can be seen by the flattening of the curve.

COVID-19 Diagnostic Tests – Current Situation

1. Nucleic Acid Testing

Since the spread of SARS-CoV-2 into the Australian population, testing for the virus has initially been focused on NAT methods (most often using the Polymerase Chain Reaction, RT-PCR technique) in the acute crisis phase to aid and confirm a positive diagnosis among symptomatic people. The five-day moving average number of tests peaked on April 1st at 14,400 per day and is currently sitting at around 6,400 per day.

NAT testing is always evolving and currently the majority of this testing is performed in a mix of private laboratories (collecting samples through the network of authorised collection centres) and public laboratories (operated by state public health systems, often in state public hospitals).

Point of care molecular testing, a growing segment of the diagnostic capability, is widespread in Australia. While the low through-put of point of care devices does not add substantial capacity, it does provide testing for regional and remote communities. There is no MBS reimbursement for point of care diagnostic assays at present, limiting the roll out and utilisation to state and territory funded services. This is a critical point for healthcare in Australia. We can now make structural changes by establishing and funding a formal point of care testing infrastructure. The benefits include better access to healthcare for regional and remote Australians, better quality of care and lower costs for patient transfer and hospitalisation.

A COVID NAT Capability Audit performed by Pathology Technology Australia has found that there is a combined capacity in accredited pathology labs to perform around 60,000 tests per day. This is over and above the non-COVID testing.

NAT has enabled effective testing in the acute phase and will remain the principal standard for diagnosing COVID-19. However, there exist inherent challenges that include:

- Availability and consistent supply of quality reagents and associated consumables from manufacturers could be a problem given global testing demands.
- NAT, depending on the technology, has varying levels of throughput and turnaround times; from 5 minutes to 6 hours for a result and from a few hundred samples per day to thousands.
- Some labs still employ manual procedures for NAT sample preparation and for testing. But an increasing number employ automated sample preparation platforms to aid throughput.
- SARS-CoV-2 viral loads in the respiratory tract can be highly variable.
    - Results can be dependent on the quality of the swab specimen taken – good contact between the swab and the back of the nose or throat is essential for maximum recovery of material for testing.
    - Results can also depend on the timing of the sample collection related to the phase of infection.

2. Serology Antibody Testing

The body's natural defensive immune response to pathogens is to produce antibodies to help fight the infection. The immune system firstly develops IgA and IgM antibodies followed by IgG antibodies which can remain in the blood stream for years following infection.

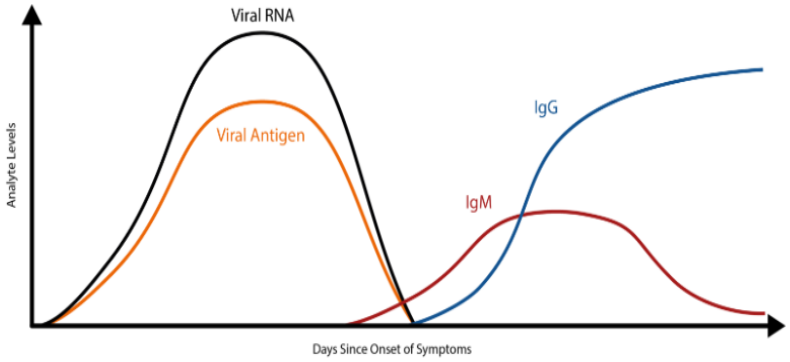

Table from Native Antigen3. Estimate of general biomarker levels during the typical time course of COVID-19/SARS-CoV-2 infection. Data from Liu et al. and Li et al 1, 2. Please note that this is purely illustrative and should not be used as a primary reference.

As depicted in the graph above the viral antigens and host antibodies arise at different times during the infection lifecycle. The virus and its associated antigens are first to rise and to be detected. Antibodies of different clases rise and fall at different times. The IgA class (associated with the nose and throat, not depicted above), are relatively non-specific but react very quickly and stimulate the sneezing reflex. The IgM class arise between 5 and 10 days after initial infection and are directed at the specific (viral) antigens. These decline and are unmeasurable after the infection is resolved. The IgG class is the last to rise and confers longer term immunity. In the case of COVID-19, we don't yet know for how long the IgG class will be effective or whether the immunity is wholly protective.

Antibody testing to aid diagnosis and patient management is an accepted standard of care in Australia and globally for numerous viruses and pathogens e.g. Hepatitis B, Hepatitis C, HIV, Rubella, Syphillis, Varicella and Epstein Barr Virus to name a few. Data on the antibody response to COVID-19 infection is still limited. Studies demonstrate the presence of IgM and IgG COVID-19 antibodies from as early as day 5 following infection [1, 2,3].
Studies have also demonstrated the combined use of antibody testing with NAT testing can reduce false negative rates compared to NAT alone[4].

Following the release of their NAT tests, pathology technology manufacturers are now finalising the development of antibody tests, both IgG and IgM, to help with global efforts to fight the COVID-19 pandemic. These antibody tests are being developed in multiple formats to address various testing needs across community settings globally. Performance of antibody tests, as measured by sensitivity and specificity, will vary depending on the test format; with high throughput, laboratory based, automated Enzyme Immuno Assay (EIA) and Chemiluminescent Immuno Assay (CLI) methods manufactured to high quality standards.

Pathology Technology Australia has completed a COVID serology capacity audit and has demonstrated ample spare capacity in testing systems to allow for large scale automated COVID-19 antibody testing to be carried out. It is estimated that over coming months, as serology test kits become routinely available, testing in the current labs could surpass 500,000 tests per day.

Serology Capability	Installed Base	Public	Private	Test results /24hrs	Capacity for COVID-19
Automated CLI Platforms	460	180	280	2,067,960	516,990
ELISA Assays	80	40	40	100,000	25,000

High quality digital point of care antibody tests, using lateral flow will also become available in Australia in coming months. Such tests promise antibody results within

15 minutes. These tests could form part of the National Testing Strategy, especially in time critical applications and for regional and remote services.

However, a word of warning about point of care lateral flow antibody tests for COVID-19: These products vary greatly in performance and even the best products can have a relatively high false positive and false negative rate. Depending on the quality systems of the manufacturer and the training level of the end user, their performance can vary from lot to lot and from user to user respectively. A significant weakness of the products currently available is their failure to capture or transmit results to a database. WHO and RCPA, amongst others, have recommened caution around the use of the current lateral flow devices. There needs to be greater certainty around the performance of these devices. We endorse state and federal agencies validating performance of current lateral flow devices prior to contracting for supply.

Proposed National Testing Protocol for COVID-19 Recovery

It is our recommendation that a combination of NAT and serology testing be adopted as front-line testing for the Australian population. We recommend a strategy for initial viral NAT and Serology testing for antigen and antibodies, in simultaneous collections of nose/throat swab and venepuncture blood test. The combination of NAT and serolgy testing, performed by the existing accredited laboratory infrastructure, reduces uncertainty and improves diagnostic sensitivity and specificity to the point where it **provides the Sentinal testing** during the recovery phase.
The introduction of high quality immunoassays that detect antigen or antibody is an important addition to use as an adjunct to diagnosis and for the ongoing diagnostic monitoring of COVID-19 infections.
This strategy also leverages the existing sample collection infrastructure. Currently there are 6149 licensed collection centers, collecting around 170,000 samples per day. These collection centers are located in all city and most regional centers. The staffing of these centres can be scaled up or down to meet demand.

Supply of high quality serology tests are available in Australia for the exisiting EIA testing platforms and are now being introduced for high volume, automated CLI platforms. These supplies, from both the USA and Europe will attenuate sovereign supply issues that might develop.
The following recommendations are proposed for population groups for COVID-19 antibody testing:

Group 1. On initial presentation of potential COVID-19 cases - add COVID-19 antibody tests to existing NAT testing to improve the initial diagnostic accuracy.

Despite the significant reduction in COVID-19 cases over the last two weeks the pending advent of the 2020 influenza season and the requirement for a differential diagnosis will ensure the continuation of molecular COVID-19 in combination with serology testing. Estimated numbers of at least 50,000 antibody tests per month.

Group 2. Re-testing of confirmed positive COVID-19 individuals & negative NAT symptomatic individuals where high likelihood of COVID-19 infection was suspected. Potential of 68,000 antibody tests per month for a 6-month period.

Group 3. Six monthly (or more frequently if needed) testing of at-risk front-line healthcare workers such as the 470,000 nurses, midwifes and medical staff across Australia. This would equate to approximately 78,000 antibody tests per month.

Group 4. Six monthly testing of essential services personnel such as the more than 126,400 law enforcement and defence forces personnel across Australia. This would equate to approximately 21,000 antibody tests per month.

Group 5. Six monthly testing of vulnerable at-risk groups such as elderly population and patients with pre-existing chronic conditions such as CVD (4.6 million individuals) & COPD (490,000 individuals). Total potential of antibody 780,000 tests per month. As a group of patients with existing chronic conditions, this group will already be presenting for routine pathology collections and testing. COVID-19 antibody testing could be performed at the same time.

Group 6. Workforce testing which could include workers in essential industries who have been exposed to the wider community or those under lockdown but need to return to normal society. Total Australian workforce is comprised of (F/T 8.9 million and P/T 4.1 million) people. Potential subset of 20% of workforce (minus healthcare workers as per item 3) equates to approximately 210,000 antibody tests per month. This will include workers in such diverse areas as schools, transport, logistics, agriculture, mining and major league sporting teams.

Group 7. Testing of blood donors to identify COVID-19 IgG positive individuals to collect COVID-19 convalescent plasma for investigation as treatment for hospitalised infected individuals. (To be agreed with ARCBS).

Group 8. Epidemiology assessment to understand community immunity. This could include targeting of asymptomatic individuals who are post- 14-day quarantine or isolation and the targeting of known geographical areas of infection "hotspots".

Group 9. Pre- and Post-vaccination testing for the appropriate administration of a vaccine which is expected to be in short supply.

Group 10. Inbound travellers from outside Australia. A separate testing strategy needs to be developed for these individuals which could be conducted prior to travel or upon arrival. The aim of this would be to safely reduce the quarantine period.

Total potential test demand between the months of June and December is summarised in the table below (Groups 1-6).

Group	June	July	August	September	October	November	December
1	50,000	50,000	50,000	50,000	50,000	50,000	50,000
2	68,000	68,000	68,000	68,000	68,000	68,000	68,000
3	78,000	78,000	78,000	78,000	78,000	78,000	78,000
4	21,000	21,000	21,000	21,000	21,000	21,000	21,000
5	780,000	780,000	780,000	780,000	780,000	780,000	780,000
6	210,000	210,000	210,000	210,000	210,000	210,000	210,000
TOTAL	1,207,000	1,207,000	1,207,000	1,207,000	1,207,000	1,207,000	1,207,000

Quality Considerations

Pathology Technology Australia consults and cooperates strongly with the TGA. Our member suppliers fully comply with global quality standards and are audited to those standards frequently. All testing devices proposed for this strategy have already or will soon have met the requirements for registration on the ARTG. In addition, we are working with an expert panel of scientists and clinicians in Australia to establish recommended performance characteristics for COVID-19 serology testing. Post-market surveillance of COVID-19 serology tests provided by Pathology Technology Australia members will provide independent evidence of their devices meeting the agreed performance requirements.
Data published so far on performance of the automated serology devices is excellent; showing extremely high sensitivity and specificity.
It is important that we clearly communicate the difference in these tests from the poor-quality lateral flow antibody tests. Regrettably the poor-quality tests attract media attention, which can diminish perception of quality for the entire sector.

Demand and Supply Considerations

Governments across the world have announced plans to introduce large scale antibody testing programs to aid decisions to commence the path back to economic and social stability. This will create unprecedented simultaneous global demand for

antibody testing kits as governments apply pressure and influence on diagnostic suppliers to ensure their testing needs are met first.

To ensure timely access to enough antibody tests to facilitate Australian's path back to more engaged economic and social participation, the Australian Government must decide on a policy for COVID-19 antibody testing and announce its intentions. To their great credit, our pathology technology supply companies have maintained supply of COVID-19 testing products. This is despite disruptions and delays in airfreight services impacting deliveries.

As a sector, we will continue to push hard to maintain adequate supplies.

To assist in this government should consider using its influence globally, and, working closely with local business partners that have a global presence, secure Australia's supply of diagnostic antibody tests from companies domiciled in countries delivering diagnostic R&D innovation. The risk of not doing so carries the potential for prolonged shortage of diagnostic materials with its subsequent community and economic effects. The promise of advance funding commitments could be persuasive in ensuring such a supply.

Local Diagnostics Innovation

Several local diagnostics innovation companies (some of whom are members of Pathology Technology Australia) are very important to our future healthcare capabilities. Indeed, some of these have innovative tests applicable to COVID-19. We must, as a country strongly support the development and commercialisation of local innovation. These have the potential to provide ground-breaking solutions to healthcare requirements into the future; as well as providing employment and export earnings. However, it is highly unlikely, and possibly commercially unsound, to think that we could be self-sufficient in producing our testing needs in Australia. This is always going to be a partnership between the larger global companies (with presence in Australia) and local partners.

Awareness Campaign

Pathology Technology Australia will work with government groups at state and federal level to provide information on testing technology and protocols. Such an awareness campaign will reduce the fear of testing – both for COVID-19 testing and amongst those with chronic illnesses who have stopped attending to their healthcare plans. It will increase trust and confidence amongst Australians, which may spill through to greater compliance with tracking and tracing and attending to their non-COVID healthcare requirements.

Government Budget Considerations

The supply of antibody tests at the volumes necessary to implement effective population health management should learn from the experience implementing funding for the PCR tests. Public Health Laboratory Network (PHLN)s were able to draw on existing resources to quickly develop in-house tests to run on existing infrastructure; however, the original MBS reimbursement level for COVID NAT tests was inadequate to enable private laboratories to compete for supply against massive global demand. The MBS reimbursement was adjusted appropriately, which ensured testing could take place.

In the case of antibody tests, a combination of government procurement commitments, well-funded public laboratories and private laboratories incentivised via MBS reimbursement will be critical to ensure Australia can obtain a timely supply of antibody tests. This will play a key part in the controlled and appropriate return to economic and social stability.

Based on the current MBS reimbursement for the COVID PCR test, and assuming;

- A new reimbursement for point of care NAT in line with the current lab item.
- A separate reimbursement for laboratory COVID Serology tests, at a level that allows us to compete for supply with the USA and Europe; suggest $50.
- A new reimbursement for point of care serology test in line with the lab item (which includes the point of care operational costs).

We estimate that the National Testing Strategy will cost between AUS$1 and 2 Billion. Best estimate is AUS$1.6 Billion. This excludes the cost of structural and process changes required to establish point of care testing services in Australia.

Such a commitment should be considered against the ongoing costs of suppressing economic activity and the budget impact of income support programs.

Summary

- Pathology Technology Australia, on behalf of the major manufacturers and suppliers of NAT and Serology tests, strongly recommend that the Commonwealth, the States and Territories quickly agree on a National Testing Strategy for COVID-19 Recovery and communicate this widely.
- This testing strategy should use a combination of NAT and serology tests to increase diagnostic accuracy and reduce time to diagnosis.

- This testing should be performed within the current pathology infrastructure and at the point of care by healthcare professionals.
- All COVID-19 test data will be captured (for example by laboratory information management systems) and used in conjunction with tracking and tracing programs and the mobile phone app (proposed by the Federal Government). The strategy proposed here enables collection and long-term storage of COVID-19 testing data.
- There is significant capacity within the current pathology testing infrastructure to complete the suggested serology and NAT workload.
- All new testing devices must be registered on the ARTG and must meet agreed quality performance characteristics; if necessary, submitting tests for assessment at the Doherty Institute (NAT), the National Reference Laboratory (Serology) or other suitable service.
- Changes will be required to facilitate and fund a point of care testing network; for COVID-19 and the longer-term healthcare of Australians.
- Governments must quickly announce the National Testing Strategy and signal commitment to the major suppliers in order to maximise the inventory of testing coming into Australia.

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About Pathology Technology Australia

Pathology Technology Australia Ltd is the peak industry body representing manufacturers and importers of technologies, vital to testing patient samples in the clinical laboratory, in hospitals and in the community.
We represent the suppliers providing 90% of all serology testing and between 65 and 85% of the suppliers for NAT sample preparation and testing.
This technology enables more than 500 million tests to be perform in Australia every year.
Pathology Technology Australia is the only entity in Australia to hold an integrated picture of the installed base of all pathology testing platforms, including the total throughput and capacity of these systems. In addition, we hold the knowledge of test availability for existing and new technology. We also hold glimpses of innovations which may be available into the future.
In the current pandemic and with an aging population and increasing disease chronicity, pathology technology will play an increasingly important role in

providing high quality, accessible and affordable healthcare services in Australia's future.

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