The Royal College of Pathologists of Australasia
ABN 52 000 173 231

Durham Hall 207 Albion Street Surry Hills NSW 2010 Australia
Telephone 61 2 8356 5858 Facsimile 61 2 8356 5828

RCPA
The Royal College of Pathologists of Australasia

Position Statement

Subject:	**COVID-19 Antigen and Point of Care Testing**
Approval Date:	30 September 2020, June 2021, August 2021
Review Date:	June 2022
Reviewed By:	Board of Directors
Number:	2/2020

Introduction

The Royal College of Pathologists of Australasia (RCPA) oversees the quality of diagnostic testing in Australia and New Zealand. The College highlights that COVID-19 rapid antigen tests (RATs) are less accurate than gold standard Polymerase Chain Reaction tests (PCR) or nucleic acid amplification tests (NAATs) (which they are sometimes referred to) which have been the highly-successful mainstay for diagnosing CoVID-19 infections in both countries throughout the pandemic. The use of highly-sensitive, specific, timely, high-throughput PCR testing has been critical to the successful public health response in Australia and New Zealand during the CoVID-19 pandemic. RCPA remains concerned that uncontrolled use of RATs is not indicated while the prevalence of SARS-CoV-2 remains generally low and may compromise our public health response. However, the College recognises that governments and public health authorities fighting localised outbreaks may need to use RATs for surveillance testing in defined circumstances as adjuncts to definitive mainstream PCR testing. By being cognisant to the limitations of RATs, the College aims to assist authorities in making the limited use of RATs for surveillance testing in CoVID-19 hotspots as effective as possible.

PCR Tests remain the preferred test for diagnosing CoVID-19 infection

PCR tests are highly sensitive and specific, and remain the preferred method for COVID-19 diagnosis. Rapid PCR tests are also available for use for urgent results but their throughput and reagent supplies remain limited. RATs were deployed into use in Europe and the United States at the height of the pandemic in 2020, particularly when the diagnostic laboratories were overwhelmed and turnaround times (TATs) became unacceptably long. Fortunately laboratories in Australia and New Zealand continue to provide reliable high-throughput PCR testing with over 100,000 CoVID tests performed daily in NSW alone.

RATs are less accurate than PCR

- Unlike PCR tests that detect gene segments of the SARS-CoV-2 virus, RATs are immunoassays that detect proteins from the virus.
- **Most importantly, RATs are less able to detect SARS-CoV-2 when present (ie. RATs are inherently less sensitive than PCR tests).** Compared with PCR tests, the sensitivity of RATs in symptomatic patients has been reported to be 72-79% (Dinnes et al., 2021) and dropping to 40-74% for asymptomatic patients – ie. **missing about 1 in 2-4 truly-infected infectious individuals** (Dinnes et al., 2021; Taylor-Phillips and Dinnes, 2021). RATs are therefore more likely to cause false-negative results, which is critical when performed in a low prevalence setting, leading to

patients with active COVID-19 infection being missed and remaining infectious in the community.

- The specificity of RATs (the ability to correctly generate a negative result for people who don't have SARS-CoV-2) is reasonably high (about 99%) (Dinnes et al., 2021), however, very few have undergone stringent evaluation. Notwithstanding, **in a low prevalence population such as Australia and New Zealand, there is potential many of the positive results will be false positives generating confusion in the community and require a second mid-nasal swab for follow-up PCR testing**
- RATs still require collection of a mid-nasal swab. Some RATs are able to give a result within 15-30 minutes.
- Some RATS require specific devices to read the results, which increases their accuracy but increases their TAT and cost.
- Unlike PCR tests, RATs are 'single patient' tests that cannot go on high-throughput automated systems, therefore they are not scalable to be used on a large population, in addition they are subject to variations in operator technique and interpretation. Lack of training and use in uncontrolled environments can lead to unreliable results.

Proponents of antigen testing postulate that mass surveillance through frequent use of the less-sensitive RATs may detect SARS-CoV-2 infection more (or as) quickly as infrequent use of the superior PCR test. This strategy has some rationale where SARS-CoV-2 infections are widespread, such as the US and UK in 2020. A mass surveillance program using RATs was conducted in Liverpool, UK, in November 2020. The results were recently published in the *British Medical Journal*. The accompanying editorial (Taylor-Phillips and Dinnes, 2021) contains the following two pertinent sentences:

- "The most important question about community mass testing is whether it works to reduce transmission. Unfortunately, we do not yet know the answer"; and

- "Further studies are urgently needed to ascertain whether population mass testing using lateral flow tests has any impact on transmission and to measure the harms of this massive scale screening."

There is even less evidence supporting mass surveillance by RATs in Australia and New Zealand where only limited independent evaluations of these tests have been performed in our populations with a low prevalence of CoVID-19. Hence the College's continued note of caution regarding RATs and our advocacy for an initial limited rollout as part of well-supervised feasibility studies.

RATs have several impracticalities that must be addressed

- Self-collected and self-administered RATs are not approved for use in Australia or New Zealand . A mid nasal swab therefore must still be collected accurately, and the RAT performed by a skilled and trained operator.
- The RAT test does not inactivate the virus and therefore represents a biohazard. Operators require appropriate personal protective equipment (PPE) and access to suitable waste disposal.
- RAT results must be recorded in the subject's medical records, and positive and negative results reported to public health authorities so that accurate tracking of the CoVID-19 pandemic can continue.
- Due to the high likelihood of false-positive results, even in a COVID-19 hotspot, all positive RAT tests must be verified by a PCR test. Due to the extraction buffer used in RATs, nasal swabs tested by RATs are unsuitable for PCR testing. A second nasal/throat swab must be collected and forwarded to a diagnostic laboratory for PCR testing.
- In addition to isolating the RAT-positive individual while awaiting the definitive PCR test result, the appropriate interim response at the testing site, which might

be a school, nursing home, medical facility or similar institution or work site, must be pre-determined and acceptable to public health authorities.
- The RAT kits must be transported, stored under appropriate temperature conditions, rotated to remain within expiry date and otherwise handled correctly at each non-clinical test site, and this handling documented.
- Each test site should participate in a registered quality assurance program (QAP) conducted at quarterly intervals.
- RAT testing is for surveillance screening and must never be used for diagnostic purposes in a symptomatic patient where a false-negative result may provide unwarranted reassurance and lead to ongoing community transmission.

Therapeutic Goods Administration Guidance

The Therapeutic Goods Administration (TGA) has updated their guidance regarding supply, training and supervision requirements for RATs (Therapeutic Goods Administration, 2021). The College agrees that health practitioners must ensure all persons performing the test under their supervision (including sample collection and interpretation of test results) are appropriately trained in all matters related to good testing practice including:

- infection control practices, including assessment of any site specific work, health and safety risks;
- the collection of samples, or where applicable the supervision of self-collection in order to verify patient identification, sample collection, test performance and test results;
- the correct use of the device and interpretation of test results;
- protocols for recording results and requirements for notification of positive results;
- protocols and referral processes for recollection and confirmatory testing; and
- protocols for reporting any problems or adverse events associated with performance of the test, including false negative or false positive results, to the Therapeutic Goods Administration.

Possible Use of RATs

RCPA recommends that, as applies to all other quality diagnostic tests, a RAT is chosen dependant on demonstration of acceptable performance in independent validations conducted under local conditions, in addition to being feasible and addressing the practical issues listed above. The College understands that various scenarios for RAT testing are being considered. These scenarios may include:

- Suspected outbreaks of COVID-19 in remote settings where PCR molecular testing is not readily accessible. Results would need to be confirmed by PCR molecular testing.
- To support PCR confirmed outbreak investigations. (ie closed or semi-closed groups including schools nursing homes, cruise ships, prisons etc). The RAT result could be used to quickly isolate positive cases and initiate contact tracing while awaiting definitive PCR testing.
- To monitor trends in disease incidence in communities particularly among essential workers such as healthcare workers during outbreaks or in regions of widespread community transmission.
- Where there is widespread community transmission, frequent antigen testing (daily or second daily) may be useful for early detection and isolation of positive cases in health facilities, nursing homes, prisons, other institutions & essential worksites, if regular, routine screening with PCR methods is not available.

Conclusion

The RCPA highlights the lower sensitivity and specificity of RATs, which therefore should never be used alone for diagnostic purposes. Authorities may need to use RATs for surveillance purposes in circumscribed agreed settings in COVID-19 hotspots. RCPA Fellows could contribute to RAT selection and other deliberations to aid in their

implementation into the Australian and New Zealand context. It is acknowledged that better performing RATs may be developed in the future. These will be assessed and commented on at that time.

References

Dinnes, J., Deeks, J., Adriano, A., Berhane, S., Davenport, C., Dittrich, S., Emperador, D., Takwoingi, Y., Cunningham, J., Beese, S., Dretzke, J., Ferrante di Ruffano, L., Harris, I., Price, M., Taylor-Phillips, S., Hooft, L., Leeflang, M., Spijker, R. and Van den Bruel, A., 2021. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database of Systematic Reviews*, Issue 3. Art. No.: CD013705.

Taylor-Phillips, S. and Dinnes, J., 2021. Asymptomatic rapid testing for SARS-CoV-2. *BMJ*, p.n1733.

Therapeutic Goods Administration (TGA). 2021. *Applying for TGA assessment of a COVID-19 test for inclusion in the ARTG*. [online] Available at: <https://www.tga.gov.au/applying-tga-assessment-covid-19-test-inclusion-artg#conditions> [Accessed 6 August 2021].