

CDGN, PHLN and CDNA Sampling Strategy for SARS-CoV-2 Genomic Surveillance

Publication history

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1.0	9 November 2021	First published

Background

Genomic sequencing has become a critical part of SARS-CoV-2 surveillance globally. Genomic sequencing may be used to:

- monitor transmission dynamics
- identify lineages with concerning features such as variants of concern (VOC)
- monitor new introductions
- link with key metadata to inform public health responses, including epidemiologic and vaccination data.

To date, Australia has employed a comprehensive sequencing strategy facilitated by low incidence of SARS-CoV-2. The [National Plan to transition Australia's National COVID-19 Response](#) has highlighted the expected increase of case numbers across the country in the short-to-medium term. In jurisdictions where case numbers have increased, the approach for genomic surveillance needs to change from *comprehensive sequencing to selective and targeted sequencing*. This balances:

- the use and cost of real-time SARS-CoV-2 genomic surveillance where there is rapid spread of a dominant strain of the virus, and
- ability of the genomic data to show variations in clusters, given the relative stability of the SARS-CoV-2 genome.

It is likely that new importations with greater genomic diversity will increase as international travel recommences. Jurisdictions with low COVID-19 case numbers may continue with a comprehensive sequencing strategy, but should consider the utility of genomic sequencing and sequencing capacity in their situations.

A robust sampling and sequencing strategy will support timely and accurate information from SARS-CoV-2 genomic surveillance. Data needs to:

- be representative,
- enable new introductions to be identified, and
- provide reliable findings that impact on public health action.

Jurisdictions will have different priorities and capacities which may change over time. It is important to have some guiding principles when selecting a sample for genomic surveillance. This will ensure a nationally consistent approach that is also broadly consistent with international guidelines.

Jurisdictions should also consider extra testing and surveillance requirements based on their local epidemiology, when developing their strategy. More information is available in the [Testing Framework for COVID-19 in Australia](#) and the [Australian National Disease Surveillance Plan for COVID-19](#).

Purpose

The Communicable Diseases Genomics Network (CDGN), Public Health Laboratory Network and the Communicable Diseases Network of Australia (CDNA) developed this document to guide Australian

public health authorities and laboratories to design and carry out a SARS-CoV-2 genomic surveillance sequencing sampling strategy. This guidance provides the principles and key characteristics of a national approach to genomic surveillance. Each jurisdiction must develop and update a sampling plan that meets the changing needs of their local epidemiological response. This guidance will be updated as needed to align with Australia's evolving epidemiological context and to be consistent with international best practice.

Objectives for SARS-CoV-2 genomic surveillance in Australia

The main objectives of SARS-CoV-2 genomic surveillance in Australia are to:

- accurately monitor the prevalence and spread of circulating strains to guide public health action,
- respond to specific outbreaks to identify sources of infection and related cases over wide geographic areas,
- detect novel or emerging variants of concern or variants of interest,
- support epidemiological and genomic virological characterisation of variants,
- understand implications for virus transmissibility and disease severity,
- understand implications for post-infection immunity, vaccine use and effectiveness,
- monitor the potential impacts of variants on diagnostic assays, and
- contribute to the global knowledge base.

National SARS-CoV-2 representative and targeted sampling approach

The national approach to SARS-CoV-2 genomic surveillance in Australia will follow two complementary sampling approaches:

1. **Non-targeted (representative) sampling** of SARS-CoV-2 nucleic acid amplification test positive cases from existing, population-based surveillance systems.
2. **Targeted sampling** of SARS-CoV-2 positive cases occurring in special settings or populations (outbreaks, vaccine breakthrough infections, travellers, etc).¹

Samples for sequencing should meet the sample criteria (see Table 1) so they're higher-quality samples, likely to be successfully sequenced. In very specific cases (focused questions of public health significance), other samples may be selectively sequenced (for example samples with higher Ct values).

Table 1. Sample-based criteria for sample sequencing selection

Criteria	Measure
Lower cycle threshold (Ct) values	Samples with low SARS-CoV-2 polymerase chain reaction (PCR) Ct value e.g. <30-32 or equivalent (as defined by jurisdictions). <i>Note:</i> Samples with higher Ct values may need to be included for monitoring the impact of variants on diagnostic assays
Age of sample	Collection date < 4 weeks.
Adequate volume	To be defined in each jurisdiction depending on sequencing methods e.g. ≥300µl.

Non-targeted (representative) sampling

Sequencing of representative or non-targeted samples (that is, randomly or systematically selected samples) should be the cornerstone of SARS-CoV-2 genomic surveillance. Ensure that the non-targeted sampling is broadly representative of the underlying population under surveillance (Table 2). Select isolates for sequencing that are broadly representative of geographic location, age groups, and sex. Isolates from all major epidemiologic clusters must be included (identified by epidemiologic clustering data) (Table 2).

Table 2. Case characteristics for representative sampling

Case Characteristic	Identified By	Data Source
Geographic location	Residential postcode or collection site	Primary diagnostic laboratories
Age groups	DOB	Primary diagnostic laboratories
Sex	Patient's sex	Primary diagnostic laboratories
Representation of epidemiological clusters (where available)	Epidemiological cluster data	Public Health Units

Targeted sampling

Targeted sampling to characterise and investigate outbreaks occurring in the targeted priority groups supports epidemiological investigations and informs public health actions. (These include high-risk settings, international arrivals, reinfection or infection in vaccinated populations). Results detected in sequencing of non-targeted (representative) sampling may also inform targeted sampling.

Consider the suggested priority groups in Table 3 for targeted sampling. The relative value of these priority groups will differ between jurisdictions and over time. This list is a guide and a suggested starting point for jurisdictional laboratories and public health units, to help to decide on the priority groups, given how important they are in each jurisdiction at that time.

Table 3. Suggested priority groups for targeted sampling

Priority Group	Justification
All international arrivals with COVID-19, and quarantine workers	Monitor introductions of SARS-CoV-2 (including VOCs/Variant of Interest (VOIs); identify quarantine breaches
Infection in vaccinated individuals	Monitor vaccine effectiveness; integrate with vaccination data to inform vaccination and infection control policies
Severe disease (patients admitted to hospital and/or intensive care unit (ICU))	Represent more severe cases; may identify strains with increased disease severity
Suspected healthcare-acquired infections	Identify roles of community vs healthcare acquisition; guide infection control policies in hospitals
Suspected re-infection cases	Identify cases of re-infection, and potential role of virus factors (lineage or sub-lineage) vs host factors (for example waning immunity, comorbidities)
High-risk settings, for example aged care, disability services, education, childcare	Targeted investigations where requested to inform PH policies for high-risk settings
High-risk priority groups, for example patients on treatment, immunocompromised patients	Identify the presence of SARS-CoV-2 virologic changes with antiviral and other treatments, and compare viral sequences/lineages to treatment responses
High-risk locations or introductions into new communities, for example regional areas, remote or indigenous communities	Identify likely sources of introduction to new and high-risk locations such as regional and remote communities

For jurisdictions with low COVID-19 case numbers, extra priority groups may include investigation of cases with:

- unknown acquisition source
- suspected interstate acquisition or
- specific outbreak investigations.

This list is likely to evolve over time, along with the needs of COVID-19 control.

Decide which priority groups to include for targeted sampling at a particular time point. Consider:

- agreed priorities of the jurisdictional public health unit (PHU). Consider national priorities to inform public health actions
- COVID-19 case numbers and sequencing capacity
- transmission status in the jurisdiction (for example unknown source cases may be informative in areas with low case numbers)
- genomic diversity present in population (for example, clonal outbreak vs multiple circulating lineages)
- availability of metadata to identify priority groups
- ability of laboratories to identify priority samples for sequencing.

Depending on each jurisdiction's situation, some priority groups may be adequately represented in non-targeted sampling. Others require more concerted efforts from laboratories to ensure adequate samples are available for sequencing to inform public health efforts.

Implement processes to avoid sequencing of non-contributory samples, to maximise the efficient use of sequencing capacity. For example, sequencing repeat patient samples, multiple samples from the same household, or multiple samples from established epidemiological clusters.

Alternative sampling strategies, such as sentinel surveillance (similar to that used for influenza) may be introduced in future. Review sequencing strategies to incorporate this.

Strategy implementation considerations

Implementing the sequencing sampling strategy will depend on:

- public health response needs
- laboratory capacity and processes across primary diagnostic laboratories and public health laboratories (or other sequencing laboratories) and
- structures to support data requirements at public health units and national policy levels.

Representative and targeted sampling levels may synchronise over time to levels of COVID-19 activity in different jurisdictions.

Laboratory considerations

- Sample selection and referral process: consider two main strategies:
 - *Complete referral* – referral of all positives to sequencing laboratory, with sample selection performed at the sequencing laboratory (based on agreed strategy with PHU). This is recommended as the most comprehensive strategy for sample ascertainment and central biobanking but is resource-intensive for both primary laboratories and sequencing laboratories. Consider the relative capacities and resources.
 - *Selective referral* – select samples at the primary diagnostic laboratory based on the sampling strategy. This should also be guided by discussion with the jurisdictional sequencing laboratory/ies to ensure a consistent approach. Only consider selective referral if any further samples require sequencing can be readily retrieved and referred to the jurisdictional public health sequencing laboratory/ies. Or, refer all samples to the sequencing laboratory/ies.
- Decide on mechanisms to quickly identify priority groups for targeted sequencing.
- Sample storage: storage duration of samples at primary and public health/sequencing laboratories, and considerations for biobanking processes.
- Sample size: calculate sample size based on a proportion of total cases. Consider sequencing capacity to meet sensitivity threshold for genomic monitoring of SARS-CoV-2 variants.

- Diagnostic assay considerations: choose samples to avoid bias from pre-screening of samples using specific RT-PCR assays to identify variants of concern.

Coordination between public health laboratories and public health units

- Public health laboratories (PHLs) and PHUs in each jurisdiction should liaise closely to identify priority groups for sequencing, design and implement a sequencing strategy for their jurisdiction, according to local needs. Review and update the strategy based on mutual agreement.
- Two-way sharing of metadata between the PHL and PHU is critical.
- Access to case epidemiological data is needed to assess whether the non-targeted sampling is representative.
- Discuss priorities for genomic sequencing with public health laboratories, based on the capacity of the sequencing laboratory.

National policy and program considerations

- Laboratory sample storage recommendations and requirements (through National Pathology Accreditation Advisory Council (NPAAC)).
- National biobanking approach for SARS-CoV-2 samples.
- Sharing jurisdictional sampling strategies at the national level to support information sharing and understanding of consistencies and differences across jurisdictions.
- Consider the following published guidance:
 - [Testing Framework for COVID-19 in Australia](#)
 - [Australian National Disease Surveillance Plan for COVID-19](#)
 - [CDNA National guidelines for public health unit: Coronavirus Disease 2019 \(COVID-19\)](#)

References

1. European Centre for Disease Prevention and Control. Guidance for representative and targeted genomic SARS-CoV-2 monitoring – 3 May 2021