Memorandum

To:	Respiratory, Infectious Diseases, Infection Prevention and Control, Molecular, Microbiology and Specimen Registration teams
From:	Chris Mansell, clinical microbiologist
Date:	18 May 2022
Subject:	SARS-CoV-2 CT (cycle threshold) values

We are now able to report CT values as a routine test, when requested. These are used to determine how much virus is present in a nasopharyngeal swab.

CT values reported for a single specimen differ between test methods and between laboratories, but with the use of standardised commercial assays they can now be used for clinical management. We do not yet have an international reference standard to quantitate viral loads, so numerical CT results are given for named brand assays. This is the number of PCR cycles before the target genes were detected. Values are typically between 10 and 45 cycles.

Recommended Applications of SARS-CoV-2 CT Number

Application / Indication	Diagnostic Criteria	Other key information required	Clinicians
Recognition of primary diagnosis when there is incidental COVID test positivity: Influenza, sepsis, pneumococcal, meningococcal or S. aureus disease This will become more common in months to come, as a large proportion of patients presenting with other conditions have recent but irrelevant COVID-19 and persistent weak positive PCR tests.	Acute sepsis or Influenza like illness. History of clinical COVID like illness or past positive test > 2 weeks previously	Blood culture, PCT, Pneumococcal Antigen (Urine). Specific Influenza Virus PCR NPS swab, in addition to COVID ID NOW swab or RAT. Past colonisation with resistant bacteria (MRSA, ESBL).	ED, Respiratory, Medicine, Paediatrics
Determination of infectious status when there is a history of past clinical COVID illness Usually, deisolation can be determined by reference to guidelines and time since infection.	Patient in hospital History of clinical COVID like illness or past positive test > 2 weeks previously Current weak positive (high CT) SARS-CoV-2 PCR	Documentation of previous past result if available. Current Respiratory and COVID clinical illness status and time course	Infection Prevention and Control

Diagnosis of Persistent SARS-CoV-2 Infection (PSI)	High levels of virus (low CT) more than 2 weeks into the illness.	Date of onset of illness Immunosuppression. Serological response	Respiratory, Infectious Diseases, Immunology
Monitoring PSI	Previously characterised PSI Stability or change in CT value	History of antiviral and immunotherapy Previous CT value with the same assay.	Respiratory, Infectious Diseases, Clinical Microbiology
Recognition of reinfection or mutation for sequencing and characterisation of immune escape variants	Documented past infection, generally > 2 months previously or continuous PSI > 2 months. High viral load (low CT) out of keeping with time frame	History of vaccination, travel, contact with travellers, immunosuppression and antiviral or immunotherapy	Respiratory, Infectious Diseases, Clinical Microbiology

Waikato Hospital de-isolation guidelines that don't require CT value (12 May 2022):

https://intranet.sharepoint.waikato.health.govt.nz/RefDocs/COVID-19%202022/Release%20of%20hospitalised%20patients%20from%20COVID%20isolation.pdf

Technical considerations: How accurate is the CT value reported ?

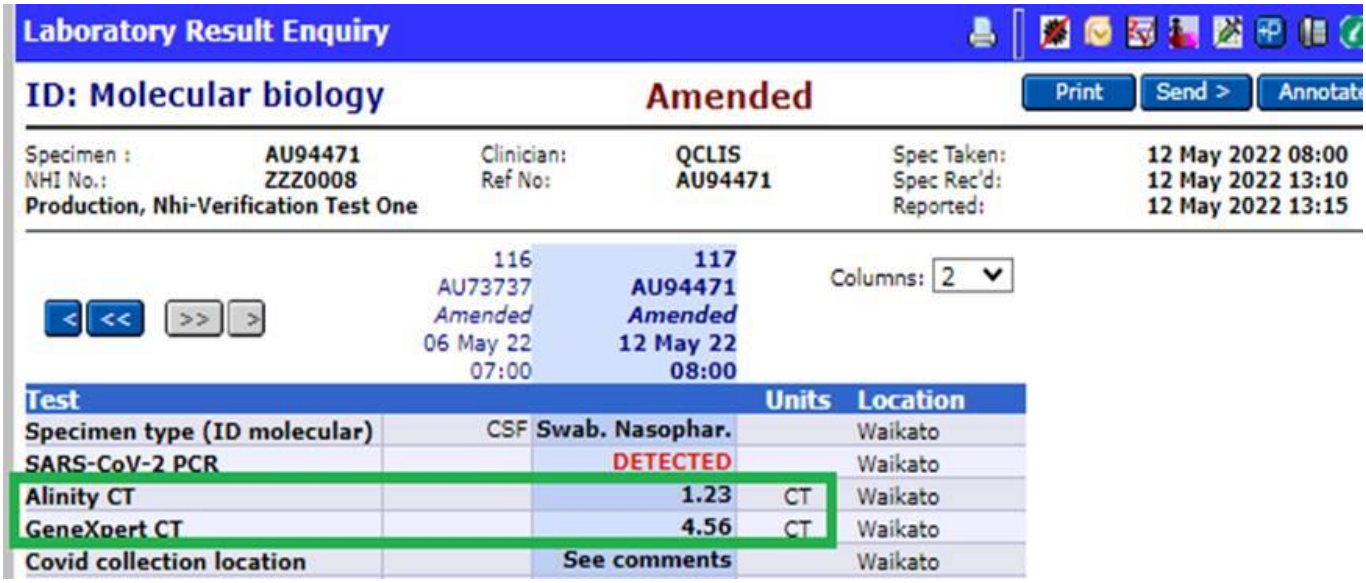
The most widely used assay is the Cepheid GeneXpert®. This uses uniform commercial reagents in cartridge form and the same amplification machine, wherever in the world it is run. About 95% of repeat tests on a sample will give results within ± 3 cycles. This will be the minimal detectable difference in viral shedding.

The other highly standardised assay in use at Waikato Hospital is the Abbott Alinity m®. This is fully automated, with uniform reagents provided by the manufacturer and run in the same machine each time. Repeat testing on a small number of samples also found that retesting will give a result ± 3 cycles in our hands. Direct comparison between the same samples tested by Alinity and by GeneXpert shows that the Alinity is more sensitive. Alinity detects the virus 3 cycles earlier than GeneXpert and samples with a CT > 37 on the Alinity are generally not detected by GeneXpert.

Result Presentation

- The CT number will be reported as a numerical value for tests "Alinity CT" or "GeneXpert CT".
- A comment will alert clinicians to the difference in values from the two methods.
- "SARS-CoV-2 CT values are 3 cycles lower on Alinity m than on GeneXpert."
- Clinical interpretation will not be offered.

Sample appearance of CWS report:



Laboratory Result Enquiry

ID: Molecular biology — Amended — Print | Send > | Annotate

Specimen : AU94471 | Clinician: QCLIS | Spec Taken: 12 May 2022 08:00
NHI No.: ZZZ0008 | Ref No: AU94471 | Spec Rec'd: 12 May 2022 13:10
Production, Nhi-Verification Test One | Reported: 12 May 2022 13:15

< << >> > | Columns: 2

Test	116 AU73737 Amended 06 May 22 07:00	117 AU94471 Amended 12 May 22 08:00	Units	Location
Specimen type (ID molecular)	CSF	Swab. Nasophar.		Waikato
SARS-CoV-2 PCR		DETECTED		Waikato
Alinity CT		1.23	CT	Waikato
GeneXpert CT		4.56	CT	Waikato
Covid collection location		See comments		Waikato