Briefing

Updated position on testing for COVID-19 using saliva as a sample

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To:	Hon Chris Hipkins, Minister for COVID-19 Response		

Contact for telephone discussion

Name	Position	Telephone
Shona Meyrick	Deputy Chief Executive (acting) – COVID-19 Health System Response	s 9(2)(a)
Darryl Carpenter	Group Manager – Testing and Supply	s 9(2)(a)

Minister's office to complete:

☐ Approved ☐ Decline ☐ Noted

☐ Needs change ☐ Seen ☐ Overtaken by events

☐ See Minister's Notes ☐ Withdrawn

Comment:

Updated position on testing for COVID-19 using saliva as a sample

Security level:	IN CONFIDENCE	**Date:**	8 July 2021
To:	Hon Chris Hipkins, Minister for COVID-19 Response		

Purpose of report

1. The purpose of this report is to provide information on the Ministry of Health's (The Ministry) updated position on testing for COVID-19 using saliva as a sample.

Summary

2. The Ministry has been assessing the role of testing for COVID-19 using saliva as a sample for some time. By April 2021, the Ministry had become confident enough in saliva as a sample that the recommendation was made to roll it out to border workers at a higher frequency.

3. Since then, evidence reviewed by the Ministry further increased our confidence in testing for COVID-19 using saliva as a sample and we have revised our position to reflect this. The Ministry is now confident that in some surveillance situations, testing for COVID-19 can be carried out using saliva samples instead of nasopharyngeal swabs.

4. A prototype of the border work roll out is currently underway, however to date there has been very low uptake. The updated position will allow changes to be made to the prototype to improve uptake, which will inform the wider roll out testing for COVID-19 using saliva as a sample across New Zealand.

Recommendations

We recommend you:

a) **Note** that the Ministry has continued to assess emerging evidence and information on testing for COVID-19 using saliva as a sample **Yes/No**

b) **Note** that the Ministry is increasingly confident that some methods of testing for COVID-19 using saliva as a sample are equivalent to testing of nasopharyngeal swabs, and that it is not necessary to complement high frequency testing using saliva as a sample with nasopharyngeal swabs **Yes/No**

c) **Note** we have adjusted the prototype of testing border workers for COVID-19 using saliva as a sample currently underway in Canterbury based on the updated position, which we anticipate will increase uptake. **Yes/No**

d) **Note** the work underway that will further inform further consideration of saliva as a sample as part of the public health response to COVID-19 in New Zealand, as well as future work on exploring a mandatory testing regime using only saliva samples **Yes/No**

Shona Meyrick
Deputy Chief Executive (acting)
COVID-19 Health System Response
Date: 7 July 2021

Hon Chris Hipkins
Minister for COVID-19 Response
Date:

Updated position on testing for COVID-19 using saliva as a sample

Background

5. The Ministry of Health has been assessing the role of using saliva as a sample for testing for COVID-19 for some time. Evidence had shown that testing for COVID-19 using saliva samples was not as sensitive as nasopharyngeal swabs, meaning there was the potential for missed infections. A single missed infection could have a significant effect in New Zealand, where there is a very low prevalence of COVID-19, and potentially lead to widespread community outbreaks.

6. By April 2021, the Ministry had become confident enough in saliva as a sample that the recommendation was made to roll it out to border workers at a higher frequency, albeit with a regular nasopharyngeal swab to mitigate any associated risks with a lower sensitivity test.

7. Since then, the Ministry has continued to review emerging science and validation studies by New Zealand and overseas laboratories, which have provided further confidence in saliva as a sample. Based on these, the Ministry is updating its position on testing for COVID-19 using saliva as a sample.

The Ministry now has greater confidence in testing for COVID-19 using saliva as a sample

8. The Ministry has reviewed several sources of information, emerging science and validation studies that has increased its confidence, including:

    a. **International literature on using saliva as a sample** – literature reviewed by the Ministry's COVID-19 Science and Insights team confirmed that saliva samples perform similarly to nasopharyngeal swabs for the detection of SARS-CoV-2. Appendix One summarises two systematic reviews that are considered of sufficient quality to inform the Ministry's position and a list of the evidence reviewed.

    b. **Validation work by local laboratories** – New Zealand based laboratories continue their own work to validate saliva as a sample and achieve International Accreditation New Zealand (IANZ) accreditation to ISO 15189 (specifically using saliva as sample). IANZ has accredited 10 laboratories to ISO 15189 (specifically using saliva as a sample) at the time of writing. Validation work reviewed by the Ministry has been carried out on limited numbers of samples, and includes but is not limited to:

        i. One laboratory has achieved accreditation to ISO 15189 (specifically using saliva as sample), with validation that shows 98.0% concordance with nasopharyngeal samples, a sensitivity of 96.6%, and a specificity of 98.6%. This test has received United States Food and Drug Administration Emergency Use Authorisation (FDA EUA).

ii. Another has also achieved ISO 15189 (specifically using saliva as sample) and uses a range of FDA EUA authorised assays that are 100% specific and sensitive and demonstrated analytical equivalency between nasopharyngeal swabs and saliva samples.

c. **Position of the New Zealand Microbiology Network (NZMN)** – The NZMN released a statement in March 2021 that recommended that if introduced, regular testing for COVID-19 using saliva as a sample for surveillance among border workers should not replace nasopharyngeal swabbing already in place. The NZMN continues to discuss saliva testing and other strategies for detection of SARS-CoV-2. While the NZMN continues to support saliva testing as a surveillance strategy alongside nasopharyngeal swabs, they also support:

i. pilot studies to collect data on the use of frequent saliva testing in place of weekly or fortnightly nasopharyngeal swabs for border worker surveillance as modelling shows that strategy would be effective

ii. pilot studies to collect data on the use of saliva testing for diagnosis of symptomatic low-risk people in the community for whom a nasopharyngeal swab is not possible to collect or where barriers to symptomatic community surveillance using nasopharyngeal swabs exist.

As a result of new evidence and information, the Ministry has revised its position on testing COVID-19 using saliva as a sample

9. The Ministry is now confident that there are surveillance situations where testing for COVID-19 may be carried out using saliva samples instead of nasopharyngeal swabs. Such situations include:

a. where frequent testing of border workers can potentially identify cases earlier, before chains of transmission are generated

b. for low risk community patients where saliva may be a better tolerated alternative to nasopharyngeal swabs and encourage more people to get tested, thus reducing the risks of missed cases.

10. This supports the need for increased testing of the border workforce as they become vaccinated. There is compelling evidence that as vaccinated individuals are less likely to be symptomatic if infected, and therefore less likely to seek a test outside of the regular testing regime, it is important that the frequency of surveillance is increased.

11. Any diagnostic testing for COVID-19 should be done using nasopharyngeal or dual oropharyngeal / nasal swabs, as there is a potential for lower amount of RNA present in saliva or lower quality saliva samples that cannot be countered by increased frequency in a diagnostic setting. Any positive test for COVID-19 via a saliva sample will need to be confirmed via a nasopharyngeal swab.

The updated position has an impact on the prototype currently underway in the Canterbury Region

12. In May 2021, the decision was made to roll out testing for COVID-19 using saliva as a sample to those working at the border. Using saliva as a sample allows testing to be carried out more frequently, especially as border workers get vaccinated and are less

likely to be symptomatic if positive for COVID-19 and are therefore less likely to seek a test.

13. A prototype has been underway in Canterbury since 28 June 2021 and will run for four week. The lessons from this will inform the wider national roll out. In preparing for the prototype, persons conducting a business or undertaking (PCBUs) and workers raised several issues with the proposed regime, that ultimately have led to an expected low uptake of saliva testing. These issues include:

    a. unwillingness of border workers to give samples outside of work hours and the impact of testing on rostered time off

    b. concerns about lowering the efficacy of testing and increasing risk by moving away from the existing nasopharyngeal based testing regime which has been much heralded as the "gold standard"

    c. the perception by workers on a seven-day cycle that participation in saliva testing would be a direct one for one swap of nasopharyngeal swabs for saliva tests

    d. complex and irregular shift patterns making compliance with a higher frequency testing regime difficult for border workers

14. The updated position will however enable changes to be made to the wider roll out to improve the uptake of testing for COVID-19 using saliva as a sample, by removing the need for a nasopharyngeal swab and simplifying the testing regime.

15. The Ministry is preparing additional advice on a change to the COVID-19 Public Health Response (Required Testing) Order 2020, for the purposes of the prototype only, to put in place a saliva-only regime and remove the requirement to have a regular nasopharyngeal swab. A briefing and draft amendment order will be provided in the week beginning 19 July 2021.

Other work is underway that will further inform the utility of testing for COVID-19 using saliva as a sample as part of the public health response in New Zealand

16. This includes:

    a. **The Surveillance Strategy** – the current review will recommend that we dynamically change surveillance settings in response to the overall balance of risk from increasing travel in the context of higher vaccination coverage, and the results of the validation studies of saliva testing. Updates to the Surveillance Strategy ultimately provide the foundation for any mandatory saliva testing regime at the border.

    b. **Further understanding of the use of saliva testing internationally** – New South Wales have been using daily saliva testing for border workers for some time. The Ministry has reached out to its New South Wales counterparts to gain a greater understanding of their regime, to inform decisions around our own introduction of saliva testing at the border.

    c. **Ongoing validation of saliva as a sample** – panels of saliva samples collected by ESR at JetPark have been provided to four laboratories in the network for analysis If the results for the analyses by the laboratories show close agreement this will contribute to greater confidence in the methods in use for a saliva-testing. The results of this verification work are expected during July.

17. This work and the learnings of the prototype will also inform future work exploring a mandatory testing regime using only saliva samples.

Next steps

18. The Ministry will begin to reflect this position in future work on saliva testing, and ensure it is well communicated across the health and disability sector. In addition:

    a. the prototype which began on 28 June 2021 will run for a total of four weeks, following which an update will be provided on the findings

    b. the Ministry will continue to engage with border agencies, PCBUs and workers to increase uptake in the prototype

    c. a briefing and draft amendment order will be provided in the week beginning 19 July 2021, following drafting by the Parliamentary Counsel Office.

Appendix One – International literature on testing for COVID-19 using saliva as a sample

Several systematic reviews have been published comparing various samples for the detection of SARS-CoV-2 to diagnose COVID-19 (listed below.) Four have been summarised below.

Study	Number of included studies in meta-analysis	Pooled sensitivity of nasopharyngeal swabs	Pooled sensitivity of saliva	Comments
Butler-Laporte, G. (JAMA) [1]	16	84.8% (95% CI: 76.8%-92.4%)	83.2% (95% CI: 77.4-91.4%)	• Adjusted pooled estimates for nasopharyngeal swabs being an imperfect reference standard
Moreira, V.M. (Diagnostics)[2]	16	Not provided	83.9% (95% CI: 77.4-88.8%)	• Diagnostic accuracy of saliva estimated to be 92.1% (95% CI: 70.0-98.3) • Mean difference of cycle threshold (CT) for saliva compared to NP was 2.792 (95% CI: −1.457; 7.041). On average, CT was higher in saliva indicating lower viral loads were observed in saliva versus nasopharyngeal swabs.
Tsang, N. (Lancet Infectious Disease) [3]	14	Not provided	85% (95% CI: 75-93%)	• Pooled specificity: 99% (95% CI: 98-99%) • Pooled positive predictive value (PPV): 93% (95% CI: 88-97%) • Pooled negative predictive value (NPV): 97% (95% CI: 94-98%)
Atieh, M. O. (Oral Diseases) [4]	16	Not provided	0.88% (95% CI 0.82–0.92%)	• Random effects meta-analytic model

References

1. Butler-Laporte, G., et al., *Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2: A Systematic Review and Meta-analysis.* JAMA Internal Medicine, 2021. **181**(3): p. 353-360 DOI:10.1001/jamainternmed.2020.8876.
2. Moreira, V.M., et al., *Diagnosis of SARS-Cov-2 Infection by RT-PCR Using Specimens Other Than Naso- and Oropharyngeal Swabs: A Systematic Review and Meta-Analysis.* Diagnostics, 2021. **11**(2) DOI:10.3390/diagnostics11020363.
3. Tsang, N.N.Y., et al., *Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis.* The Lancet Infectious Diseases, 2021 DOI:https://doi.org/10.1016/S1473-3099(21)00146-8.
4. Atieh, M.A., et al., *The diagnostic accuracy of saliva testing for SARS-CoV-2: A systematic review and meta-analysis.* Oral Diseases, 2021. **n/a**(n/a) DOI:https://doi.org/10.1111/odi.13934.

Other reviews

Kivelä, J.M., et al., *Saliva-based testing for diagnosis of SARS-CoV-2 infection: A meta-analysis*. Journal of Medical Virology, 2021. 93(3): p. 1256-1258.

Lee, R.A., et al., *Performance of Saliva, Oropharyngeal Swabs, and Nasal Swabs for SARS-CoV-2 Molecular Detection: A Systematic Review and Meta-analysis*. Journal of Clinical Microbiology, 2021: p. JCM.02881-20.

Mohammadi, A., et al., *SARS-CoV-2 detection in different respiratory sites: A systematic review and meta-analysis.* EBioMedicine, 2020. 59.

Khiabani, K. and M.H. Amirzade-Iranaq, *Are saliva and deep throat sputum as reliable as common respiratory specimens for SARS-CoV-2 detection? A systematic review and meta-analysis.* American journal of infection control, 2021: p. S0196-6553(21)00140-1.

Yokota, I., et al., *Equivalent SARS-CoV-2 viral loads by PCR between nasopharyngeal swab and saliva in symptomatic patients.* Scientific Reports, 2021. 11(1): p. 4500.