Briefing

Update on testing for COVID-19 using saliva as a sample

Date due to MO:	11 November 2021	**Action required by:**	
Security level:	IN CONFIDENCE	**Health Report number:**	20212447
To:	Hon Chris Hipkins, Minister for COVID-19 Response		
Copy to:	Hon Andrew Little, Minister of Health Hon Ayesha Verrall, Associate Minister of Health		

Contact for telephone discussion

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Minister's office to complete:

☐ Approved ☐ Decline ☐ Noted

☐ Needs change ☐ Seen ☐ Overtaken by events

☐ See Minister's Notes ☐ Withdrawn

Comment:

Update on testing for COVID-19 using saliva as a sample

Security level:	IN CONFIDENCE	**Date:**	11 November 2021
To:	Hon Chris Hipkins		

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 diagnostic sample.
2. The report also updates you on a recent review of the border workforce saliva testing roll-out.
3. This report discloses all relevant information.

Summary

4. In July 2021, the Ministry advised you that based on our assessment of emerging evidence and information on testing for COVID-19 using saliva as a sample, we were increasingly confident that that it was not necessary to complement high frequency testing using saliva as a sample with nasopharyngeal swabs (HR20211563). Based on this, a recommendation was made to roll out saliva to the border workforce at a higher frequency with the rollout beginning on 11 August 2021.
5. The Ministry recently commissioned a review of the border workforce saliva testing rollout to assess the success of the programme. The review focussed on operational aspects and identified several areas for improvement. However, it generally found that there was unanimous support for saliva testing being available as an option for the border workforce.
6. The Ministry has continued to assess the emerging evidence and information on COVID-19 testing, including using saliva as a sample type. We are now confident that using saliva as a sample tested by Nucleic Acid Amplification Testing (NAAT) is an equivalent alternative to a nasopharyngeal swab by NAAT for diagnosing COVID-19. When ESR has completed validation of whole genomic sequencing for saliva, confirmation by a nasopharyngeal swab will no longer be needed for positive saliva samples.
7. The updated position on COVID-19 testing, using saliva as a sample is consistent with the newly developed Testing Strategy.

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 confident that using saliva as a sample test by Nucleic Acid Amplification Testing (NAAT) is equivalent to testing of nasopharyngeal swabs by NAAT — **Yes/No**

c) **Note** that some surveillance situations may require an increased frequency of testing depending on the risk situation **Yes/No**

d) **Note** that a saliva sample tested by NAAT is an alternative to a nasopharyngeal swab by NAAT for diagnosing COVID-19 **Yes/No**

e) **Note** that when ESR has completed validation of whole genomic sequencing for saliva, a confirmation by nasopharyngeal swab is no longer needed for positive saliva samples. **Yes/No**

Bridget White
Acting Deputy Chief Executive
COVID-19 Health System Response
Date: 10/11/2021

Hon Chris Hipkins
Minister for COVID-19 Response
Date: 13/11/2021

Update on testing for COVID-19 using saliva as a sample

Background / context

8. In July 2021, the Ministry advised you that based on our assessment of emerging evidence and information on testing for COVID-19 using saliva as a sample, we were increasingly confident that that it was not necessary to complement high frequency testing using saliva as a sample with nasopharyngeal swabs (HR20211563).

9. In August 2021, saliva as a sample type tested by Nucleic Acid Amplification Test (NAAT) started being offered to the border workforce as an alternative to nasopharyngeal swabs. Border workers who have opted-in are required to submit their saliva sample as a series of 2 tests within 7 days at least 2 days apart.

10. During the Delta outbreak, most permitted workers who need to cross Alert Level boundaries to work at a permitted business must get a COVID-19 test or have a medical examination within the previous seven days. Permitted workers crossing the Alert Level boundaries around Auckland who have opted into using saliva as a sample type are also required to submit their saliva sample as a series of 2 tests within 7 days at least 2 days apart.

The Ministry has reviewed the emerging science and validation studies

11. The Ministry has continually reviewed emerging science and validation studies, domestic and international, of saliva as a sample. These include:

    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.

        i. Appendix One summarises the evidence and links to 11 systematic reviews.

        ii. In a published longitudinal study, saliva had similar sensitivity to nasopharyngeal swabs when tested weekly; 96.3 percent compared to 98.7 percent, respectively. Increased frequency of testing, irrespective of the sample type or technology, increases the performance of the test and likelihood of detecting SARS-CoV-2.

    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 percent concordance with nasopharyngeal samples, a sensitivity of 96.6 percent, and a specificity of 98.6 percent. 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 equivalence between nasopharyngeal swabs and saliva samples.

c) **Updated position of the New Zealand Microbiology Network (NZMN)** – The NZMN released a statement on 16 September 2021 that recommended saliva could potentially be an alternative sample type for use as a diagnostic test for symptomatic testing when a swab is not tolerable, and where individuals would otherwise not be tested. It was noted for asymptomatic surveillance programmes, frequency of NAAT testing is an important component of SARS-CoV-2 surveillance programmes and NZMN recommends testing at least twice a week for these reasons, regardless of sample type for NAAT.

d) **International government agencies** – The US Centers for Disease Control and Prevention lists saliva as a sample type for use as a diagnostic test and as of 2 November 2021, the US Food and Drug Administration Agency has given emergency use authorisation to 31 molecular diagnostic tests using saliva as a sample type. As of 5 October 2021, the UK Medicines and Healthcare products Regulatory Agency lists saliva as an alternative sample in their guidance 'For patients, the public and professional users: a guide to COVID-19 tests and testing kits'.

As a result of new evidence and information, the Ministry has revised its position on saliva testing

12. The Ministry is now confident that saliva tested by NAAT can be used as a diagnostic test for COVID-19.

13. As of 10 November 2021, whole genomic sequencing (WGS) is only available on nasopharyngeal swabs in New Zealand. As a result, a positive saliva by NAAT will continue to need a follow up nasopharyngeal swab, not for confirmation but for WGS. Work is underway at ESR to validate saliva for WGS. Once validation has been completed, a positive result by saliva will no longer require a follow-up nasopharyngeal swab.

14. There is no pre-determined frequency in which saliva tested by NAAT should be conducted. Depending on the risk profile, there are some surveillance situations where increased frequency of testing for COVID-19 is recommended, such as:

    a) Workers in high-risk environments such as healthcare workers caring for COVID-19 patients. Frequent testing can potentially identify cases earlier before chains of transmission are generated. There is good evidence that vaccinated individuals are less likely to be symptomatic if infected. Therefore, they may be less likely to seek a test outside of the regular testing regime, and so the frequency of surveillance may need to be increased.

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

Border workforce saliva testing review

16. Saliva was approved for border workforce surveillance testing under the Required Testing Order (RTO) from 11 August 2021 and made available to the border workforce. A review of the border workforce saliva testing rollout was commissioned by the Ministry. The purpose

was to assess the success of the rollout and make recommendations for improving the current state of border workforce saliva testing and implementation of future initiatives. A summary of the review is attached as Appendix two.

17. The review found that saliva testing being a viable option for the border workforce, providing genuine choice, has unanimous support. The use of saliva as an approved sample type was not rolled out as expected for the border workforce initially, with several challenges. However, the review also noted that lessons have been learned and the current state of border workforce saliva testing is in reasonably good shape. The review also noted that the rollout of permitted worker testing was a noticeable improvement.

18. In addition to the Border workforce saliva testing review, the COVID-19 Behavioural Insights, Science & Insights team at the Ministry is completing an applied research study with Testing Operations exploring adherence to the required testing order among the maritime border workforce, specifically stevedores.

19. Preliminary results from focus group discussions with stevedores are: nasal swabs are preferred over saliva testing, but not by much; a common barrier to regular testing is the concern about testing positive; a common motivation for getting tested is a sense of responsibility to whānau; and generally, the border workforce know where and when they need to get tested at work, but don't necessarily know the closest testing station or drop-off box to their home.

20. The results of the review findings will inform future practice and work programmes.

Equity

21. The impacts of COVID-19 are felt differentially across New Zealand communities. Māori and Pacific communities and those living with disabilities, in lower socio-economic groups and crowded or institutional settings bear a greater portion of both health and economic impacts and risks.

22. COVID-19 testing, using saliva as a sample is a key part of the suite of tests available to identify COVID-19 cases and prevent the transmission of COVID-19 into the community, particularly to those communities with many essential workers and higher-risk settings. COVID-19 testing using saliva as a sample has provided a less invasive alternative to nasopharyngeal testing for surveillance testing and will continue to do so under the Ministry's updated position.

Next steps

23. The Ministry will immediately begin to make the necessary changes and promote its updated position on saliva testing through its testing work programmes.

ENDS.

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

In a published longitudinal study, saliva had similar sensitivity to nasopharyngeal swab when tested weekly, 96.3% compared to 98.7%, respectively. Increased frequency of testing, no matter the sample type or technology, increases the performance of the test and likelihood of detecting SARS-CoV-2 (Smith, R. Longitudinal Assessment of Diagnostic Test Performance Over the Course of Acute SARS-CoV-2 Infection, The Journal of Infectious Diseases, Volume 224, Issue 6, 15 September 2021, Pages 976–982, https://doi.org/10.1093/infdis/jiab337).

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	88% (95% CI 82–92%)	• 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.

Bastos ML, Perlman-Arrow S, Menzies D, et al. 2021. The Sensitivity and Costs of Testing for SARS-CoV-2 Infection With Saliva Versus Nasopharyngeal Swabs : A Systematic Review and Meta-analysis [published correction appears in Ann Intern Med. 2021 Apr;174(4):584]. Ann Intern Med. 174(4):501-510. doi:10.7326/M20-6569

Ibrahimi N, Delaunay-Moisan A, Hill C, et al. 2021. Screening for SARS-CoV-2 by RT-PCR: Saliva or nasopharyngeal swab? Rapid review and meta-analysis. PLoS One. doi:10.1371/journal.pone.0253007

Appendix Two – Summary of the Border Workforce Saliva Testing Review

1. The purpose of the review was to assess the success of the rollout of saliva testing for the border workforce and make recommendations for improving the current state of border workforce saliva testing and the implementation of future initiatives.

2. Saliva was approved as a sample method for border workforce surveillance testing under the Required Testing Order (RTO) from 11 August 2021 and made available for the border workforce. This gave the border workforce the choice to use saliva as a sample for surveillance testing for COVID-19 rather than undertake a nasal (nasopharyngeal) swab testing cycle.

3. Within a week of go live, the first community cases of the Delta variant were detected, placing the Ministry into full response mode, and New Zealand was placed into higher Alert Levels. Just over 5 weeks later, on 16 September, permitted worker testing was implemented for workers crossing the Auckland alert level boundary. The permitted worker testing leveraged heavily off the border workforce saliva testing programme.

4. The review's aim was to test two main overarching questions:
   a. Was the use of saliva as an approved sample type rolled out as expected for the border workforce?
   b. Were key performance indicators related to the implementation and uptake successfully delivered?

5. The review assessed the systems and processes that are in place, service provider performance, uptake and compliance, and user experience, in order to make recommendations for improvement.

6. The review included reviewing relevant legislation and documentation and interviews with a cross-section of stakeholders involved in border testing. This included several agencies (MoH, Maritime NZ, MBIE, MPI, MoT, Customs and DPMC), DHBs (NRHCC and HBDHB), and PCBUs (Air NZ, JetPark, CentrePort, Port Nelson, Port Taranaki), as well as APHG (Asia Pacific Healthcare Group), the National Road Forum and the Rail and Maritime Transport Union.

Summary of the Review

7. The review identified a number of high level findings and provided recommendations for consideration.

8. The review commended the Ministry team for the work they have undertaken to get the programme to its current state, acknowledging the challenges in setting up an entirely new operational process at speed across multiple sites and settings.

9. The review found that saliva testing being a viable option for border workers, providing genuine choice, has unanimous support. There was overwhelming positive feedback on the end-to-end process for workers once they are underway with saliva testing and for APHG, the service provider.

10. However, the review also found that the border worker saliva testing rollout had a rocky start with multiple parts of the programme experiencing challenges due to insufficient time, changing settings, and unclear roles & responsibilities, which led to a variety of frustrations for the Ministry of Health (the Ministry), agencies, PCBUs, the service provider APHG, and workers, and a general sense of confusion in the early stages.

11. It identified that the Ministry's initial testing regime policy position for the border workforce saliva testing, that involved saliva tests on days 3, 6, 9 and 12, together with a "close out" nasopharyngeal test on day 14, was too restrictive as a regime. It also identified that the removal of the need for the "close out" nasopharyngeal test within the saliva testing regime, which was removed just prior to the go live of saliva testing for the border workforce, was pivotal in creating a saliva testing regime that was potentially appealing for the border workforce.

12. The review suggested that there was a need for the Ministry and Border Workforce Senior Officials Group (BWSOG) to reflect on the areas of the rollout that did not go so well including the length of time it took for a viable saliva option to be made available, the issues in the engagement processes and communications, how the BWSOG could have functioned better to support the rollout, the somewhat more complex settings and processes for saliva testing, and the reasons for the low uptake of the saliva testing option to date (8.4% as at 7 October).

13. The review found that the use of saliva as an approved sample type was not rolled out as expected for border workers initially (review question 1), with a number of challenges as noted above, however the review also noted that lessons have been learned and that the current state of border workforce saliva testing is in reasonably good shape. The review also noted that the rollout of permitted worker testing was a noticeable improvement which is discussed further below.

14. The review also found that only some key performance indicators related to the implementation and uptake were successfully delivered (review question 2). The most surprising was the low uptake of saliva testing as mentioned above. However, the review also notes that it is unclear what this KPI is attempting to measure.

15. The review noted that reported compliance for saliva testing is lower than expected. As at 6 October, compliance over the preceding 7 days for saliva testing was 89 percent compared to nasopharyngeal swabbing at 97 percent compliance. Actual saliva testing compliance is expected to be higher but is impacted by reporting challenges related to the frequency of saliva tests. Other KPIs were delivered as expected.

16. The review was able to compare the border worker rollout with the next iteration of saliva testing, the permitted worker testing for crossing the Auckland alert level boundary. The review noted that this was stood up in five days from a standing start, and was notably smoother to implement, with far fewer challenges. The review highlighted that the permitted worker testing was able to leverage the learnings from the border worker saliva testing rollout and further concluded that permitted worker testing was unlikely to have succeeded as it did, had the border worker saliva testing not already been in place.

17. While the review found that the permitted worker testing rollout was successful, and that border workforce saliva testing is now working much better, it also identified areas where additional work is needed to ensure that the next testing initiative does not encounter some of the same challenges experienced in the border worker saliva testing rollout.

18. The BWSOG has considered the review and concluded that it is a fair reflection of the border workforce saliva testing and permitted worker rollouts. In particular, the BWSOG reflection was focused on improving how it operates as a group and how the policy development and operationalisation process could be improved. The BWSOG noted that these two areas were also identified by the first phase Venter review into border testing that was commissioned by the Border Executive Board (BEB).