South African Health Products
Regulatory Authority
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Communication to Stakeholders **8 September 2020**

MD024: Frequently asked questions: Performance evaluation of point-of-care COVID-19 serology antibody test kits

1. My test has been submitted for validation. What will happen next?

SAHPRA is working together with the national reference laboratory to assess tests. The assessment has two stages. The first stage looks at test performance on 25 well-characterised patients who tested positive for SARS-CoV2 and who are a median of 33 days post-infection and 25 well-characterised negative patients. In secondary validation, the panel is expanded to include 100 additional specimens. There is also repeatability testing to ensure that there is consistent performance.

2. What are the acceptance criteria for the first stage assessment?

The acceptance criteria are:

a. a sensitivity of >85% compared with PCR; and
b. a specificity of >98% compared with PCR.

The test must meet these criteria for **IgG** only against PCR.

3. These acceptance criteria seem onerous?

The acceptance criteria have been published in SAHPRA document "***MD007: Specification criteria for COVID-19 serological test kits"*** on the 22 July 2020

4. How can I be sure that the correct patients are included in the panel?

Patients which are included for the primary validation are all within the window of maximal IgG production (between day 14-40 post-symptom onset). These specimens have been standardised with respect to the number of days. Antibody presence has been confirmed by multiple platforms. This is the sample selection which should test positive on the test. Negative patients were from well-characterised sera banks stored prior to 2020.

5. My test reached a specificity of 100% versus PCR but a sensitivity <85% versus PCR but achieved a sensitivity of >85% versus lab-based serology. Can it not go onto a secondary validation?

No. The test needs to meet the criteria as compared against PCR.

6. My technical dossier suggests that total antibody performance is better than IgG alone.

This may be the case, however due to the generally poor performance of IgM, the NHLS have excluded IgM as part of the criteria. This is for a number of reasons including the fact that IgM is less likely to be produced and provides a less durable antibody response. IgM information is given for completeness and is not included in the decision-making process

7. My test fulfils the criteria for secondary validation. What happens in this process?

In secondary validation, the panel is expanded to include a 100 additional specimens. There is also repeatability testing to ensure that there is consistent performance. The criteria for recommendation of the test, remains the same as per the primary validation.

8. Are the sensitivity and specificity criteria the only ones which are considered when deciding to recommend a test for authorisation?

No. In addition, Robustness (ease of performing the test), sample requirements (fingerstick blood or venous blood) and the number of invalid test results are also taken in to account. A test may meet the sensitivity and specificity criteria but then fail on these additional product specifications. In addition, the test should analyse both IgM and IgG on a single platform.

9. I believe that my product could perform better and would like for it to be re-evaluated at the NHLS. How can this be done?

A test will only be re-evaluated if there is overwhelming data to show that there have been substantial changes in the test design or make-up. In this case, the applicant is required to make a new application to SAHPRA to list the changed test kit.

10. Who can authorise a validation?

Only SAHPRA can authorise a validation.

11. I submitted my products for validation and I still have not received a report. What is the turnaround time for reports?

The turnaround time is dependent on a number of factors including the requirements for secondary validation and in some cases field evaluation and the number of tests which are awaiting validation. We will attempt to return a report within 6 weeks but this cannot be guaranteed.

12. I would like to have my test evaluated by another laboratory. Is this possible?

No. In the interests of fairness and transparency, the process has been standardised and may only be performed at the National Reference Laboratory. This is a formal academic laboratory which subscribes to *ISO15189:2012* guidelines and is SANAS accredited. All reports are compiled by a trained medical scientist and reviewed by an expert pathologist.

13. Can I have a copy of the protocol for my records?

The protocol has been shared with SAHPRA but, for ethical reasons, neither the raw data nor the protocol itself will be shared with suppliers.

14. Will the validation report be shared?

The validation report may be shared with stakeholders including other regulatory jurisdictions, the National Institute of Communicable Diseases, clinical societies and the Department of Health.

15. Data from my suppliers indicates that the test meets the sensitivity and specificity requirement

Please note that wide variability has been noted between and even within lots from the same supplier from studies across the world. In addition, some suppliers provide multiple rapid testing platforms which, again, show variable performance. Data from outside South Africa is considered by SAHPRA to inform a decision on whether to refer the product for validation or not. SAHPRA's regulatory decision is based on data from the National Reference lab.

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