SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

Communication to Stakeholders **March 2022**

MD033: Specification criteria for COVID-19 rapid antigen self-tests

BACKGROUND

1. The COVID-19 pandemic is caused by SARS-CoV-2, a novel coronavirus that originated in Wuhan, China in late 2019. The virus has since spread around the world, with novel variants of concern causing new waves of infection.
    i. Testing is a critical component of COVID-19 control and prevention strategies. Self-testing for SARS-CoV-2 infection using antigen-detecting rapid diagnostic tests is an approach that can be used to broaden access to COVID-19 testing, alongside conventional testing methods.
    ii. COVID-19 rapid antigen self-tests provide a presumptive test result for the SARS-CoV-2 virus and are intended to be used in the home or similar environment by a lay person.
    iii. Self-test results should be used and interpreted according to the national algorithm and should not replace professional use rapid diagnostic tests or PCR testing where such testing is appropriate and available.
    iv. A positive self-test result means that the test detected SARS-CoV-2, and that the individual is very likely to have an infection and should adhere to recommended public health guidance around isolation and mask wearing etc. to reduce the spread of the disease.
    v. A negative self-test result means that the test did not detect SARS-CoV-2, but it does not rule out infection. Repeating the test within a few days, with at least 24 hours between tests, will increase the confidence that the individual is not infected.
2. SAHPRA has adopted the Australian Therapeutic Goods Administration, specification criteria for COVID-19 rapid antigen self-tests.
3. These specifications are subject to review and may need to be updated at short notice.
4. This document provides the minimal specification criteria clinically acceptable for COVID-19 rapid antigen self-tests, to be manufactured and/or distributed in South Africa during the current COVID-19 pandemic caused by the SARS-CoV-2 virus.
5. A COVID-19 rapid antigen self-tests with lower specifications than articulated in this document are likely to provide no clinical benefit and might lead to increased harm, which would be unacceptable.
6. Professional use only COVID-19 Rapid antigen self-tests which are already approved (i.e. went through performance evaluation by the National Reference Laboratory (NRL) and are authorised by SAHPRA), will not go through a full validation as per guidance document published on the SAHPRA website namely MD 015:"*Process flow – Imported COVID-19 test kits*". For abovementioned application only the following documents will be required by SAHPRA:
    a. Updated packaging details (e.g., Instruction for use and Labels) clearly showing that the product is for self-test,

b. Usability studies (both the plan and report) for application submit of product that has not been approved by the regulator (in this case, SAHPRA), as per SAHPRA usability guidance document

7. For COVID-19 Rapid antigen self-tests which are not approved for Professional use only (have not gone through performance evaluation by the National Reference Laboratory (NRL) and are not authorised by SAHPRA) will go through a full validation as per guidance document published on the SAHPRA website namely; "MD 015: *Process flow – Imported COVID-19 test kits*". Furthermore to the requirements for application submission stated in the guidance document MD 015, the applicant is required to submit the Usability studies plan and report.
8. The samples need to consist of strongly positive results, a high proportion of weakly positive results, negative and invalid results to fully assess the ability of the lay person to obtain the correct result.
    a. If the test uses an app to analyse or assist in the interpretation of results this needs to be used in the study to demonstrate there is no negative impact on interpretation, particularly for weak positive results.
    b. A significant inter-reader variability (e.g. ≥ 5%) for clearly positive or negative results implies the following on the test kit:
    c. It is not easy to use, the IFU is not clear enough, or the test may be difficult to interpret resulting in an increased rate of false negative or false positive results.

9. In defining the specification, the following classification will be applied:

Acceptable:	Defines the minimum acceptable product specification
Desired:	Highly desirable features of considerable benefit. As time is of the essence if omitting one of these features significantly accelerates development and production it should be considered
Point of care test:	An *in vitro* diagnostic medical device intended to be used by a healthcare professional or non-professional (lay) person outside of a laboratory in primary or secondary care environments

SPECIFICATIONS FOR COVID-19 rapid antigen self-tests.

10. Specifications are subject to review and can be updated.

Specification criteria for COVID-19 rapid antigen self-tests.		
These are initial specifications based on current information. These specifications are subject to review and may need to be updated at short notice.		
Key Features	**Desired**	**Acceptable**
Priority Features		
Preferred product profile	Detection of virus particle (antigen-based) Should not cross-react with seasonal or non-SARS-CoV-2 viruses.	
Target Population The person providing the sample to be tested	Asymptomatic and symptomatic virally infected individuals	
Target user setting The person operating the test kit	An individual who is capable of using the device without training, but with reference to the included labelling and instruction for use.	An individual who is capable of using the device without training, but with reference to the included labelling and instruction for use.
Clinical sensitivity [a] (false negatives – telling someone they haven't had the infection when they have)	at least 80% (for specimens collected within 7 days of symptom onset)	at least 80% (for specimens collected within 7 days of symptom onset
Clinical specificity (false positives - telling someone they have had the infection when they haven't)	Greater than 98%	Greater than 98%
Analytical sensitivity	studies to establish the limit of detection of the test and that reflect test performance using different sample types	studies to establish the limit of detection of the test and that reflect test performance using different sample types

Analytical specificity (interference and cross reactivity)	studies to demonstrate the test detects all SARS-CoV-2 strains and will not produce a false positive result due to cross-reactivity with other human coronavirus (Except SARS-CoV-1) or interference by an unrelated pathogen or substance. Studies should include non-infected individuals, potentially interfering and cross-reactive samples, and Other respiratory pathogens, including bacteria.	studies to demonstrate the test detects all SARS-CoV-2 strains and will not produce a false positive result due to cross-reactivity with other human coronavirus (Except SARS-CoV-1) or interference by an unrelated pathogen or substance. Studies should include non-infected individuals, potentially interfering and cross-reactive samples, and Other respiratory pathogens, including bacteria.
Positive Predictive Value (PPV)	at least 80%	at least 80%
Negative predictive value(NPV)	Greater than 98%	Greater than 98%
limit of detection	Acceptable: 102 – 103 TCID50/ml; Ideal: <1 x 102 TCID50/ml	Acceptable: 102 – 103 TCID50/ml; Ideal: <1 x 102 TCID50/ml
Sample type	Nasopharyngeal swab , Throat swab	Nasopharyngeal swab , Throat swab
Available Pack Size	Single/multiple packs	Single/multiple packs
Usability and User comprehension	Diagnostic sensitivity, non-supervised – at least 30 lay users that are known antigen positive • Diagnostic specificity, non-supervised – at least 60 lay users that do not know their status	Diagnostic sensitivity, non-supervised – at least 30 lay users that are known antigen positive • Diagnostic specificity, non-supervised – at least 60 lay users that do not know their status

Inter-reader variability	Inter-reader variability studies should consider the ability of at least 100 individuals to interpret Pre-determined and/or contrived results.	Inter-reader variability studies should consider the ability of at least 100 individuals to interpret Pre-determined and/or contrived results.
Test format A single use disposable, rapid diagnostic test housed in a test cassette	A standardised kit that contains all materials and equipment required for the procedure in a self-contained kit that includes controls, non-hazardous reagents and Instruction for use.	A standardised kit that contains all materials and equipment required for the procedure in a self-contained kit that includes controls, non-hazardous reagents and Instruction for use.
Test Accessories	Pack includes all accessories needed for taking sample and its application to test	Accessories are routinely available in healthcare institution environment.
Regulatory Status	Originating approval and evidence of use in jurisdictions recognised by SAHPRA	Originating approval and evidence of use in jurisdictions recognised by SAHPRA

Test Procedure		
Number of steps to be performed by operator (incubation steps) [c]	No more than 4 steps	5 or fewer steps
Need for operator to transfer a precise volume of sample or reagents	No	Acceptable if robust transfer device is provided with the test device and if variation does not affect the test results
Requirement to add reagents e.g. sample diluent / buffer	No	Diluent provided in dropper bottle
Biosafety	Design should mitigate need for special requirements to dispose test and the accessories needed to perform test No special biosafety measures should be required for self-testing	Design should mitigate need for special requirements to dispose test and the accessories needed to perform test No special biosafety measures should be required for self-testing
Disposal requirements	Dispose in household waste	Dispose in household waste
Need for operator to transfer a precise volume of sample	No	No
Time to result	No more than 15 minutes	No more than 20 minutes
Internal control	Included, procedural control detecting the capability of the assay	Included, procedural control detecting the capability of the assay
Sample preparation Need to process sample prior to performing the test	No more than 15 minutes None or fully integrated	No more than 15 minutes None or fully integrated
Invalid rate	No more than 0.1%	No more than 1%

Operational characteristics		
Stability studies	open and closed shelf-life studies for the kit (test strip, buffer) that consider the extremes of temperature and humidity that the tests may be exposed to in South Africa ; and transport simulation studies relevant to the claimed shelf-life and environmental conditions for storage, transport and use (e.g. temperature and humidity	open and closed shelf-life studies for the kit (test strip, buffer) that consider the extremes of temperature and humidity that the tests may be exposed to in South Africa ; and transport simulation studies relevant to the claimed shelf-life and environmental conditions for storage, transport and use (e.g. temperature and humidity
Operating conditions	5 - 30°C 80% relative humidity	5 – 30°C 70% relative humidity
Reagent storage (shelf life stability)	12 months at 2- 35°C No cold chain require	12 months at 2- 35°C No cold chain require
In use stability	More than 1 hour after opening of an individual pouch	More than 30 minutes after opening of an individual pouch
Reagents reconstitution Need to prepare the reagents prior utilization	All reagents and consumables provided and ready to use	All reagents and consumables provided and ready to use

Operational characteristics

End point stability (time window during which signal remains valid)	Up to 30 minutes	Up to 30 minutes
Reader to reader variation	More than 95% of readers should detect true positive results near the limit of detection	More than 95% of readers should detect true positive results near the limit of detection
Volume of sample	Dispense 3-4 drops of extracted specimen	Dispense 3-4 drops of extracted specimen
Disposal requirements	device and accessories should be disposed in a safe manner and disposal instruction attached	device and accessories should be disposed in a safe manner and disposal instruction attached
Kit presentation (if not single format)	✦ 1 Test kit ✦ Test components individually packed ✦ Accessories not too small to be used with regular examination gloves ✦ Include all required components and accessories to perform the test	✦ 1 test kit ✦ Test components individually packed ✦ Accessories not too small to be used with regular examination gloves ✦ List components required but not provided
Training needs	Minimal (IFU to provide graphics)	Minimal (IFU to provide graphics)
Power Requirements	None required	None required
Need for Calibration/ maintenance/spare parts	None	None should be require
Instructions for Use	✦ In line with Medical Device Regulation 24 requirements ✦ Simple interpretation by lay person with pictorials to aid sampling and results interpretation and what to	✦ In line with Medical Device Regulation 24 requirements Simple interpretation by lay person with pictorials to aid sampling and results interpretation and what to

	do with the test if the control fails	do with the test if the control fails
Operational characteristics		
	✦ Clear reading time and Indications for different ranges of intensity/ concentration of target antigen/antibody ✦ Clear warnings of limitations for use including expected performance characteristic ✦ Paper or electronic	✦ Clear reading time and Indications for different ranges of intensity/ concentration of target antigen/antibody ✦ Clear warnings of limitations for use including expected performance characteristic ✦ Paper or electronic
Manufacturing environment	Conforms to ISO 13485:2016	Conforms to ISO 13485:2016
Lead time for production	1 month maximum	No more than 3 months

[a] Confirmation tests could be molecular PCR test for SARS CoV 2 virus using validated laboratory test on Nasopharyngeal swab , Throat swab

[b] Assessment of cross reactivity with other pathogens (pre-pandemic samples, other coronoavirus, SARS CoV 1, EBV, RF)

High priority organisms likely in the circulating area for example:

- Adenovirus (e.g. C1 Ad. 71)
- Human Metapneumovirus (hMPV)
- Parainfluenza virus 1-4
- Influenza A & B
- Enterovirus (e.g. EV68)
- Respiratory syncytial virus
- Rhinovirus
- Chlamydia pneumonia
- Haemophilus influenza
- Legionella pneumophila
- Mycobacterium tuberculosis
- Streptococcus pneumonia

- Streptococcus pyogenes
- Bordetella pertussis
- Mycoplasma pneumonia
- Pneumocystis jirovecii (PJP) [c] Steps needed by operator e.g. preparation of reagents, lancing of finger for blood sample, adding sample to test cartridge, incubation time before reading.

DR B SEMETE-MAKOKOTLELA

CHIEF EXECUTIVE OFFICER OF SAHPRA

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