health

Department:
Health
REPUBLIC OF SOUTH AFRICA

GUIDE TO ANTIGEN TESTING FOR SARS-COV-2 IN SOUTH AFRICA

FOREWORD

The following policy guideline is intended for use by health care professionals involved in the management of Covid-19 in South Africa. The document provides guidance on diagnostic tests available, on antigen test performance and accessibility. It focuses on key issues such as when to perform antigen tests, how to use and interpret results. Capturing and reporting testing information is also covered. Clinical management of Covid-19 is covered in a separate document.

Management of Covid-19 is still an evolving strategy, and needs to be adapted through evidence-based information. This policy guideline document contains recommendations based on the most recent and available scientific evidence; however, comments and suggestions from those working in the field are essential to ensure a dynamic process, aimed towards optimal control of Covid-19 in South Africa. Please forward these to: The Team Lead Covid-19 Case Management. E-mail: Norbert.Ndjeka@health.gov.za

The National Department of Health would like to acknowledge the technical assistance and invaluable inputs made by all people who were involved in the development of these guidelines innumerable to be listed here individually. A special word of gratitude goes to CHAI, NICD, NHLS and WHO for supporting the development of these guidelines.

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Director General: Health

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1 INTRODUCTION

In July 2020, a targeted testing strategy was developed to address South Africa's testing response to COVID-19. This strategy was developed to accommodate the country's constrained testing capacity, to deal with the testing backlog, and to ensure that those categories of patients with an urgent clinical need were prioritised for testing. Symptomatic hospitalised patients, as well as healthcare workers, were therefore prioritised for testing. This guidance was updated in October 2020 for South Africa to utilise its expanded COVID-19 testing resources to support all components of the COVID-19 response.

At the start of the pandemic, only nucleic acid amplification tests (NAATs) were available for COVID-19 diagnostic testing. In October 2020, select SAPHRA approved antigen-detecting rapid diagnostic tests (Ag-RDT) were approved for use in South Africa. The development of Ag-RDTs for rapid and/or point of care identification of patients with SARS-CoV-2 infection is a helpful addition to the real-time reverse transcription polymerase chain reaction (rRT-PCR) assays due to their ease of use and rapid turnaround time.

This guide seeks to address practical considerations regarding the implementation of SARS-CoV-2 Ag-RDTs. It provides support for healthcare providers, health facility managers, casualty staff and community outreach testing teams regarding the implementation of antigen testing. The document covers all aspects of the use of the antigen test and reporting of results, and is applicable in both the public and private sectors.

2. TESTING FOR SARS-CoV-2

2.1 Tests Available for SARS-CoV-2 Diagnosis

Rapid identification of infected persons supports infection control in both hospital and community settings, provision of clinical care and timely initiation of public health

containment measures. Although the rRT-PCR assay remains the recommended method for the diagnosis of active SARS-CoV-2 (COVID-19) infection in South Africa, the need for laboratory facilities and the longer turnaround time for results may limit the ability to effectively isolate, treat, and contact trace in a timely fashion.

Ag-RDTs detect specific proteins (antigens) of replicating SARS-CoV-2 virus in respiratory specimens to diagnose current infection. Currently authorized antigen tests for SARS-CoV-2 require nasal (anterior nares) or nasopharyngeal swab samples, and most Ag-RDTs employ a lateral flow test format (commonly used for the diagnosis of other pathogens such as HIV, malaria and influenza). Tests are performed in <30 minutes and can be performed in a laboratory or at the point of care, thereby enabling faster patient care decisions, meeting testing demands in resource-limited settings, and increasing access to testing by supporting service decentralisation.

While rRT-PCR assays have a broader window of detecting SARS-CoV-2 infection and are more sensitive, Ag-RDTs can be used on pre-symptomatic (1-3 days before symptom onset) and early symptomatic phases of illness when individuals have high viral loads and are likely to be most infectious (Figure 1). Table 1 outlines the strengths and weaknesses of each test type.

Figure 1: Testing sensitivity profile based on viral concentrations during infection with SARS-COV-2. High-frequency testing with low analytical sensitivity versus low-frequency testing with high analytical sensitivity[1]

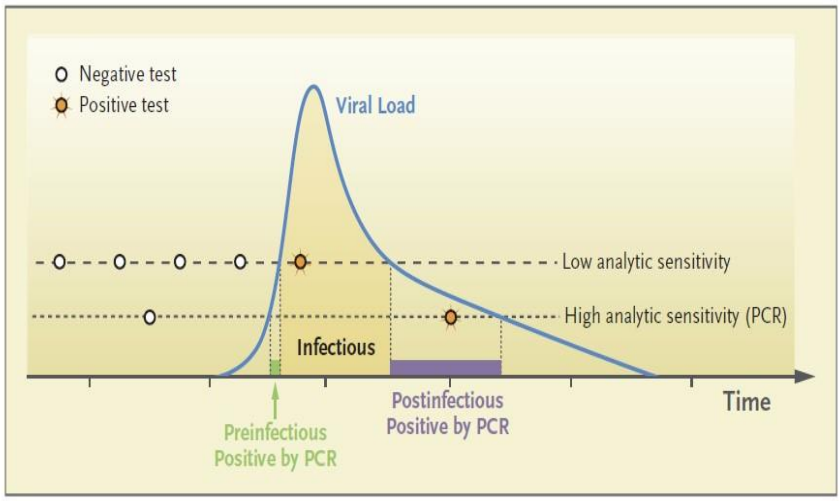


Table 1: Comparison of strengths and weaknesses of real-time reverse transcription PCR (rRT-PCR) and antigen-detecting rapid diagnostic tests (Ag-RDT) for COVID-19 diagnosis

[1] Mina, M.J. et al. Rethinking COVID-19 Test Sensitivity — A Strategy for Containment. NEJM. DOI: 10.1056/NEJMp202563

Testing method	*Strengths*	*Weaknesses*
SARS-CoV-2 rRT-PCR test	• "Gold standard" test • High **sensitivity** • High **specificity**	• **Longer turnaround times** may limit the ability to quickly isolate, treat, and contact trace • Requires laboratory facilities and may therefore **limit access to testing** • **Higher cost** ○ Requires laboratory facilities and may therefore limit access to testing
SARS-CoV-2 Ag-RDT	• **Faster turnaround** times • **Lower cost** • **Greater access to testing,** particularly in areas further away from PCR labs • Allows for **decentralisation of testing** to lower-level health facilities • **Faster identification** of cases and contacts for quarantine/isolation • Simple to perform	• Smaller window of detection • **Less sensitive** than PCR and so small number of false-negative results can occur • May require confirmatory testing under certain circumstances, **may need to be followed by a rRT-PCR test**

2.2 Antigen Test Performance and Accessibility

As per World Health Organization (WHO)[2] recommended minimum performance requirements, Ag-RDTs with ≥97% specificity and ≥80% sensitivity may be used for diagnosing infection with SARS-CoV-2, where no nucleic acid amplification tests are available or have prolonged turnaround times. A recent systematic review showed that sensitivity of Ag-RDTs varied considerably across studies (from 0% to 94%) with an average sensitivity of 56.2% (95% CI 29.5% to 79.8%) while specificity was consistently high with an average specificity of 99.5%

[2] World Health Organization, 2020. SARS-CoV-2 antigen-detecting rapid diagnostic tests: an implementation guide. https://www.who.int/publications/i/item/9789240017740

(95% CI 98.1% to 99.9%; based on 8 evaluations in 5 studies on 943 samples).[3] The sensitivity of Ag-RDTs is higher when viral loads are higher (low cycle threshold (Ct) in rRT-PCR), which is usually within the first 5-7 days following symptom onset when patients are expected to be highly infectious, therefore timing of testing is crucial.

A number of near-patient tests (or point of care tests) have been developed for rapid diagnostic purposes, and, following extensive consultation with regulatory bodies and through both the Foundation for Innovative New Diagnostics (FIND), the WHO and the United States Food and Drug Administration (FDA), a number of Ag-RDTs have been identified which show acceptable accuracy and clinical performance in the correct cohorts. The South African Health Regulatory Authority (SAHPRA) has subsequently approved a number of tests using a reliance model as well as in-country validation. These assays are constantly being reviewed and an updated list is available on the SAHPRA https://www.sahpra.org.za/medical-devices/medical-devices-and-in-vitro-diagnostics-test-kits/

3. WHEN TO PERFORM THE TEST

Ag-RDTs may be performed on all persons for whom the rRT-PCR test is indicated, where no nucleic acid amplification tests are available or have prolonged turnaround times that limit clinical or public health response utility.

Ag-RDTs are likely to perform well within the first 5-7 days of illness when viral loads are high. Patients presenting more than 5-7 days after illness onset are likely to have lower viral loads and false-negative results may occur. The positive predictive value (PPV) of Ag-RDTS is higher in settings of high SARS-CoV-2 prevalence.

3.1 Facilities eligible for testing

Optimal, quality assured Ag-RDT results are best obtained when trained staff conduct the test in a controlled environment. Antigen test kits may be available in the public and private sectors.

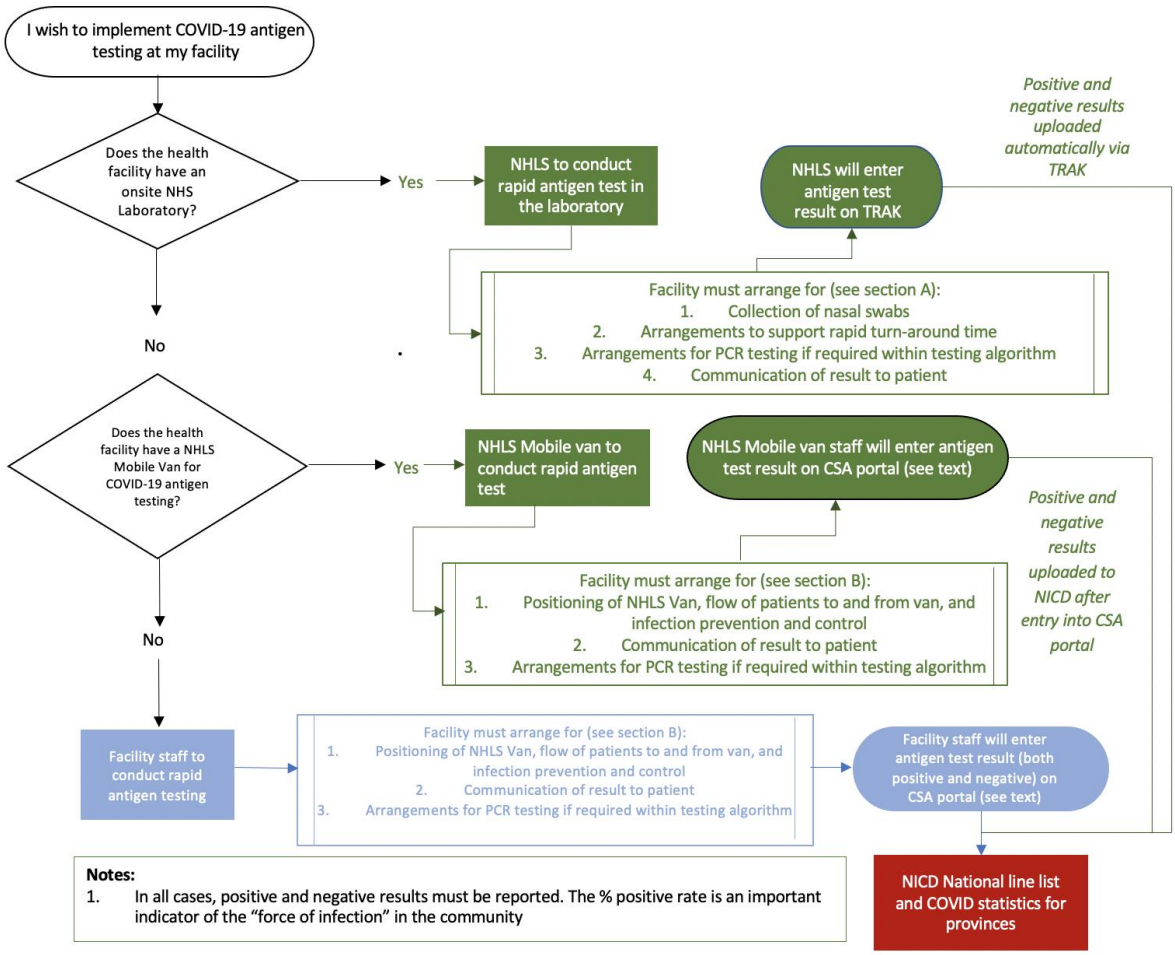
The NHLS has undertaken to support the roll-out of the antigen test in the public sector, and has made the following arrangements – see below and Figure 2:

- Where a health facility has an on-site NHLS laboratory or is provided with an NHLS mobile unit, trained laboratorians will perform the antigen test. Special arrangements will be made to support a rapid TAT.

[3] Dinnes, Jacqueline, et al. "Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection." *Cochrane Database of Systematic Reviews* 3 (2021). https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/pdf/full

- Where a health facility has neither an on-site NHLS laboratory nor an NHLS mobile unit, the NHLS will support the provision of test cartridges and training of staff assigned to conduct testing at POC.

Figure 2:Decision tree for implementation of COVID-19 antigen testing in public and private sector facilities



4. HOW TO USE AND INTERPRET RESULTS OF SARS-CoV-2 ANTIGEN TESTS

Ag-RDTs must be used in accordance with the provisions of the SAHPRA licensing conditions, including good clinical and laboratory practice (GCP, GLP) requirements. Appropriate infection prevention and control measures (IPC) should be observed when collecting specimens for testing, as patients are potentially infectious, and clinicians are at risk of contracting COVID-19.

Antigen test kits must be stored and used, by trained operators, as specified in the manufacturer's instructions to ensure optimum test performance. Ensure correct procedures for specimen collection and handling are followed as all SARS-CoV-2 tests are affected by the quality and integrity of the specimen. Quality control procedures, including testing on control specimens, must be followed to prevent cross-contamination and inaccurate results.

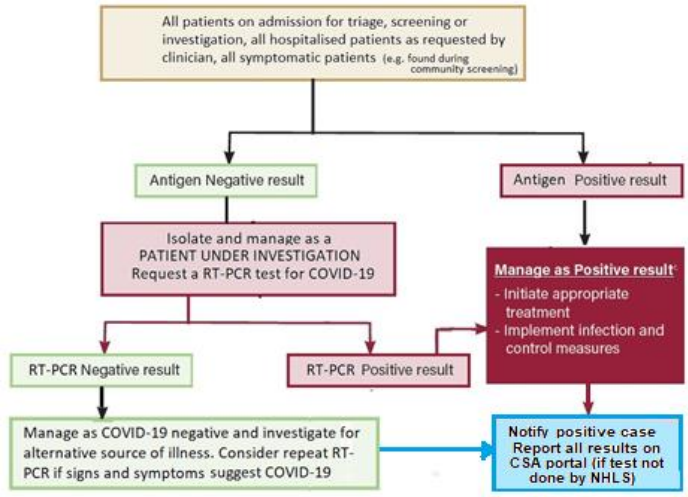
The interpretation of Ag-RDT results depends on the clinical and epidemiological context of the person being tested. Guidelines for the interpretation of Ag-RDT results are shown in Figure 3.

In some circumstances, confirmation of the Ag-RDT result with a rRT-PCR test is recommended. In high prevalence settings, in individuals presenting with clinical COVID-19 symptoms, or individuals that are close contacts of a COVID-19 case, it is recommended that a negative Ag-RDT be followed by a rRT-PCR test. In individuals with a low likelihood of SARS-CoV-2 infection or with a clinical syndrome not consistent with COVID-19, it is recommended that a positive Ag-RDT be followed by a rRT-PCR test. Confirmatory testing should be performed as soon as possible (<48 hours) after the initial test.

Step 1

Does the person have symptoms compatible with COVID-19?

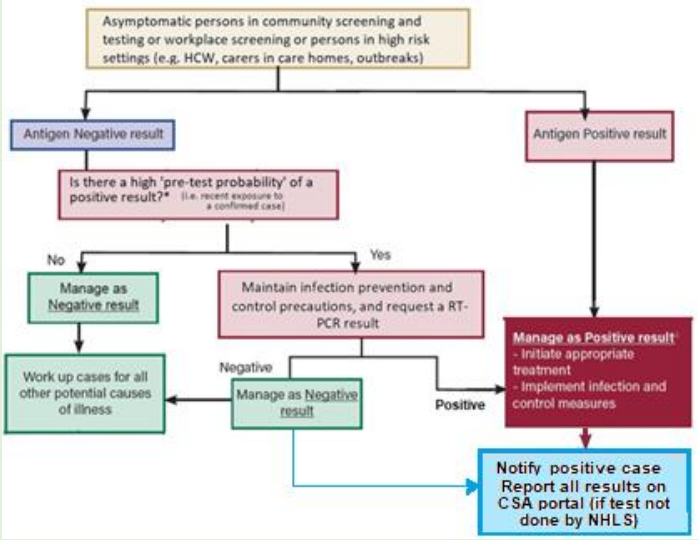
If yes
use flow-chart to the right to interpret result



Step 2

Does the person have symptoms compatible with COVID-19?

If no
Use flow-chart to the right to interpret result



Step 3
Report the result

Report ALL results (positive and negative) at https://csa.nhls.ac.za/ unless the antigen test was done by the NHLS
Positive results should be reported by the attending clinicians to the NICD as part of **Notifiable Medical Conditions surveillance** (NMC-SS). Details may be found on the NICD website at https://www.nicd.ac.za/nmc-overview/overview/

5. CAPTURING AND REPORTING TESTING INFORMATION

All SARS-CoV-2 antigen tests (both positive and negative) are required to be reported to the NHLS/NICD as soon as possible (<48 hours) after performing the test. Reporting can be done using (i) the NHLS Laboratory Information System (Trakcare) where available, (ii) directly downloaded into the NICD API, or (iii) on the web-based COVID-19 Screening App (CSA). Reporting only on positive cases will result in the country not being able to calculate an accurate positivity rate. It is therefore imperative that both positive and negative results are reported timeously.

The NHLS has developed a web-based application (COVID-19 Screening App, CSA) to capture information on tests done in the private sector or the public sector outside of a NHLS laboratory, which is non-billable. If the test is performed in an NHLS laboratory, NHLS captures information directly into the Laboratory Information System (LIS), Trakcare. Full reporting procedure can be found in Figure 4.

The results of antigen testing may be directly downloaded into the NICD API by arrangement with the NICD. This is suitable for hospital groups, pharmacies or smaller private laboratories that do not already have a data submission arrangement with NICD. Please contact Fazil McKenna (fazilm@nicd.ac.za) or Ndivhuwo Munava (ndivhuwom@nicd.ac.za) for further assistance.

SARS-CoV-2 is a Category 1 notifiable medical condition that requires immediate reporting of positive patients by a written or electronic notification to the National Department of Health (DoH) Notifiable Medical Conditions (NMC) surveillance system (https://www.nicd.ac.za/nmc-overview/notification-process/) within 24 hours of diagnosis by healthcare providers, private health laboratories or public health laboratories (the NICD provides this service for the NDoH).

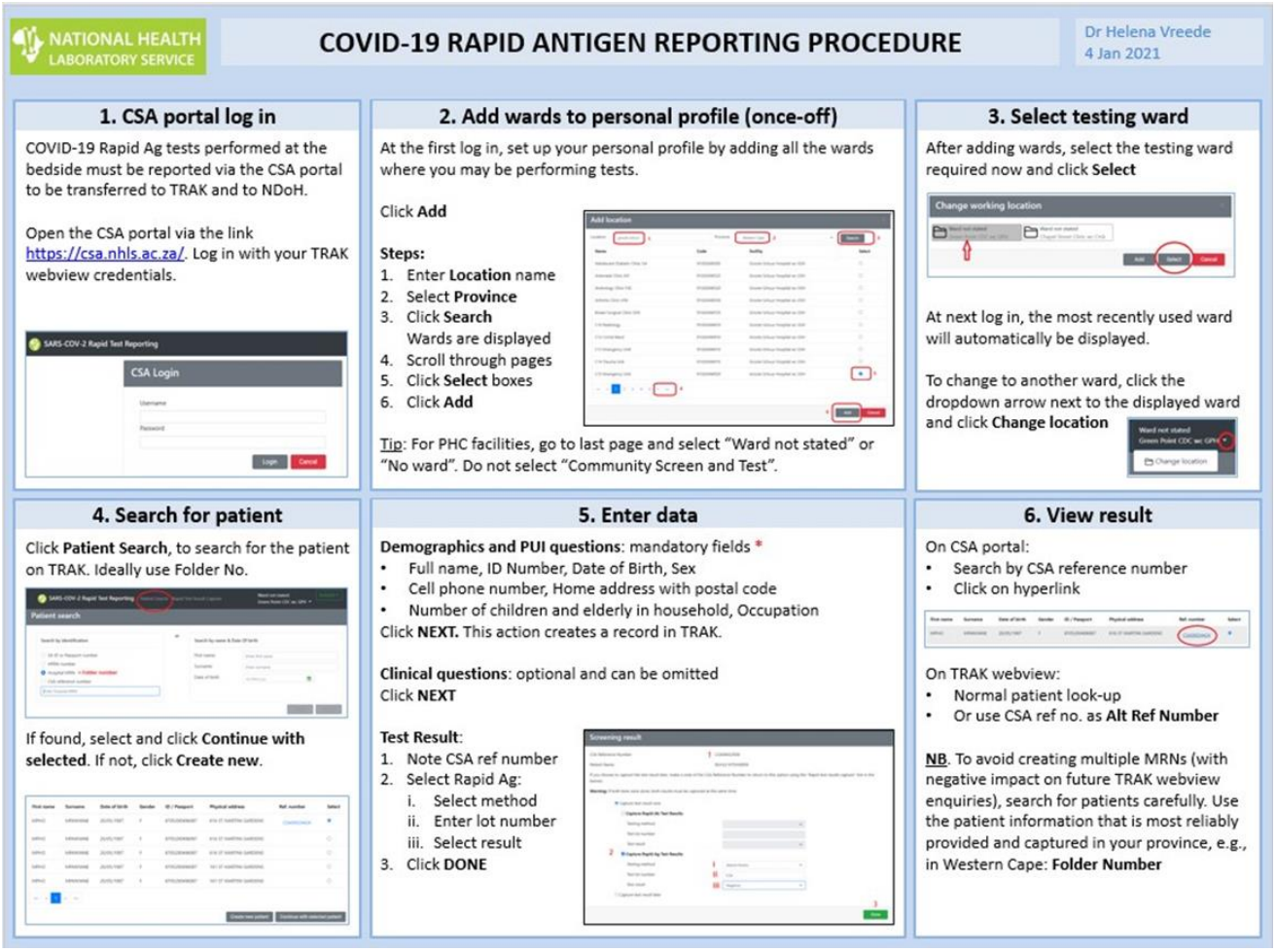


Figure 4. Procedure for reporting of COVID-19 antigen test results (both positive and negative) using the CSA portal developed by the NHLS. Private healthcare staff* and NHLS staff who are testing at ports of entry or health facilities in mobile testing vans should use this mode of data capture. (*Manual data entry is not required if data are entered into a LIS, or there is a direct data upload into NICD API)

6. APPENDIX

NHLS Area Manager contact details

Sector	Name	Role	Email address	Tel number
Eastern Cape				
NHLS	Mrs Tabita Makula	Area Manager : Eastern Cape Region	tabita.makula@nhls.ac.za	082 893 6875
NHLS	Mr Ighsaan Gamieldien	Business Manager: Nelson Mandela Bay & Sarah Baartman	ighsaan.gamieldien@nhls.ac.za	082 8095287
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NHLS	Ms.Buyiswa Ndlebe	Business Manager: Alfred Nzo & Joe Gqabi	buyiswa.ndlebe@nhls.ac.za	082 899 2351
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NHLS	See: E Rampota/ B Xhakaza (Acting)	Johannesburg, Sedibeng and West Rand		082 872 9969 /082 941 5672
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KwaZulu-Natal				
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NHLS	Mr Brian Naidoo	Business Manager: Mngungundlovu-Thukela	brian.naidoo@nhls.ac.za	082 676 4804
Limpopo				

Sector	Name	Role	Email address	Tel number
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North West				
NHLS	Mr. Jone Mofokeng	Area Manager: Free State and North West	jone.mofokeng@nhls.ac.za	082 603 2577
NHLS	Stephen Monareng	Business Manager: North West	stephen.monareng@nhls.ac.za	082 881 1313
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NHLS	Brandon Juries	Business Manager: GSH / RC	brandon.juries@nhls.ac.za	082 748 9406
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