FUNCTIONS AND MINIMUM STANDARDS FOR SUPRANATIONAL REFERENCE LABORATORIES AND REGIONAL CENTRES OF EXCELLENCE IN THE SADC REGION

NOVEMBER 2010

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**ACRONYMS AND ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
<th>Definition</th>
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<tr>
<td>AIDS</td>
<td>Acquired immunodeficiency virus</td>
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<td>ART</td>
<td>Antiretroviral therapy</td>
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<td>CDC</td>
<td>Centres for Disease Control</td>
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<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<td>ELISA</td>
<td>Enzyme-linked immunosorbent assay (synonym EIA)</td>
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<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>MDR</td>
<td>Multidrug-resistant</td>
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<td>MDG</td>
<td>Millennium Development Goals</td>
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<tr>
<td>M&amp;E</td>
<td>Monitoring and evaluation</td>
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<tr>
<td>MTCT</td>
<td>Mother-to-child transmission (of HIV)</td>
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<td>RNA</td>
<td>Ribonucleic acid</td>
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<td>SADC</td>
<td>Southern African Development Community</td>
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<td>TB</td>
<td>Tuberculosis</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>XDR</td>
<td>Extensively drug-resistant</td>
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ACKNOWLEDGEMENTS

This work was made possible through the collaboration of the Southern African Development Community (SADC) Secretariat with Member States and various stakeholders. The Secretariat would like to acknowledge all the contributions. Firstly, Member States of SADC, through their Laboratory Coordinators and other focal points, provided information about Member States programmes, and coordinated discussions with other stakeholders during the field assessments. Additionally, programme managers reviewed drafts and provided valuable technical input and guidance to the report/framework.

Senior government officials in the Communicable Diseases Project Steering Committee, National AIDS Authorities and Members of the HIV and AIDS Technical Advisory Committee reviewed final drafts and made recommendations to facilitate finalisation and subsequent approval of the document at the joint SADC Ministerial Meeting of Ministers of Health and Ministers responsible for HIV and AIDS.

This work also benefitted from collaborating partners including the United Nations Organisations, namely WHO. The SADC Secretariat would like to thank them for their technical inputs in reviewing various drafts of the document as well as participating in technical meetings to discuss the work.

The consultant for this work was Prof Elopy Nimele Sibanda who collected data from the Member States and produced a situation and response analysis report which informed the development of the minimum standards. Additionally, the consultant provided valuable technical inputs and drafted various drafts of the report.

At the SADC Secretariat this work led by the Directorate of Social and Human Development and Special Programmes under the leadership of Mr. Stephen Sianga. Specifically, the work was coordinated by the SADC Communicable Diseases Project led by Mr Innocent Modisaotsile, Project Coordinator. Colleagues at the HIV and AIDS programme and the Health Desk also contributed immensely by reviewing various drafts of the work and providing valuable feedback.

Lastly, these Minimum Standards would not have been possible if it were not for the financial support provided by the African Development Bank through their grant to the SADC Secretariat on Communicable Diseases (HIV and AIDS, TB and Malaria). Furthermore, the Secretariat would like to acknowledge financial assistance by the Joint Financing and Technical Collaboration for co-funding of the Consensus building workshop.
Figure 1: Diagramatic representation of the background and rationale for the establishment of Supranational Reference Laboratories and Regional Centres of Excellence

1. Assessment of Member States National Reference Laboratories by The SADC Secretariat (December 2008 to March 2009)
   - Major Gaps in service provision noted
   - Solutions required to address Gaps

2. Priority One: Strengthen Capacity of all NRLs

3. Establish Regional Centres of Excellence to address cross-cutting, disease Neutral aspects of Laboratory service provision:
   - Human resource development,
   - Quality Management Systems,
   - Information Management,
   - Surveillance and Research

4. Interim Measure: Provide alternate access to services:
   - Diagnostic Supranational Reference Laboratories (SNRL)
   - Disease Specific (HIV, TB, Malaria)
1. INTRODUCTION

The communicable diseases that exact the highest human and financial costs in the SADC are HIV and AIDS, tuberculosis (TB) and malaria. While it is agreed that laboratories are of central importance to communicable disease management, their functional status was shown to be encumbered with challenges.

The first challenge is the absence of a common definition of the structure, role and functions of a national reference laboratory. Without a common definition there are no common expectations. Indeed, the assessment of national reference laboratories by the SADC Secretariat reported the existence of different laboratory models with different mandates and variable operational emphasis.

The range of services did not always encompass all expectations. The services provided were also inadequate. The availability of key diagnostic tests, including the detection of resistance to HIV and TB medicines was suboptimal. Key public health functions, such as disease surveillance and epidemic preparedness, were compromised by an absence of policy direction, as well as by limitations in human and financial resources. The gaps include numbers and competencies of personnel, inadequacies in physical infrastructure and equipment, suboptimal adherence to quality practices in the performance of tests, and variable methods and monitoring and evaluation (M&E) of the performances of the laboratories. The availability of essential diagnostic tests fell below what has become standard of care in other parts of the world and the adherence to quality management practices left room for improvement.

There is an urgent need to strengthen the capacity of the laboratories to deliver on their mandates. However, this is a lengthy process. It is therefore necessary to find alternative ways of providing services while national reference laboratory capacity is being strengthened, hence the need for supranational reference laboratories.

The shortcomings observed in some Member States occur against in the background of increasing demands for certain specialised diagnostic services. These needs have to be addressed. Since a range of essential diagnostic tests cannot currently be performed within some Member States, it is essential that the services are provided elsewhere in the SADC region. This role could be played by a laboratory or laboratories with the requisite capacity and mandates to carry out trans-border diagnostic services (supranational reference laboratories). This option is envisaged by the SADC through its Protocol on Health which explicitly spells out the need “to cooperate in the establishment of regional reference laboratories and in sharing technical expertise” as one way of addressing existing inadequacies.

Supranational laboratories need to be defined, and their place and roles in service provision to Member States needs to be regularised in order to ensure conformity with the guiding SADC Protocols. This report summarises the gaps in service provision in Member States and proposes optional models of supranational laboratory services as a response. The expected functions can be grouped into two integral components: (a) diagnostic and (b) public health. The report further outlines the functions and roles of such laboratories.

Recommendations regarding the general functions, organisation, staffing profiles, coordination, and financing modalities that are anticipated for supranational reference laboratory are outlined. Specific recommendations on the specialised roles relevant to the diagnosis and public health service provision in HIV and AIDS, TB and malaria are provided.
The range of challenges faced by Member States’ national reference laboratories can only be partially addressed by supranational reference laboratories. The latter are an essential, but contingency, stopgap measure that recognises the existence of deficits that cannot be bridged quickly. The long-term strengthening of the national reference laboratories requires a fundamental audit of the causes of those deficits, and a proposal of modalities to address them.

Our assessment of the status of national reference laboratories identified four major areas of deficits, which transcend all laboratories and need to be corrected if national reference laboratories are to be strengthened. These were inadequacies in policy and in human resources; quality practices were poorly implemented, and information management systems were poorly organised and inadequately implemented.

Addressing these shortcomings is vital for strengthening national reference laboratories, but cannot be achieved alone with supranational reference laboratories. Therefore, regional centres of excellence in some of these areas are recommended. Such centres should be mandated to spearhead efforts to strengthen laboratories in concert with service provision through the supranational reference laboratories.
2. BACKGROUND

A situation analysis of national reference laboratories was carried out by the SADC Secretariat in 2008 and completed in March 2009. The purpose of the assessment was to determine the capacity of existing national reference laboratories to provide basic diagnostic services to support the management of the major communicable diseases of regional significance – HIV and AIDS, TB and malaria.

More broadly, the assessment sought to appraise the SADC secretariat of the state of preparedness of national reference laboratories to provide all necessary diagnostic and public health functions. The capacity to provide these services was referenced on regional and international guidelines on national reference laboratories. Several key areas of assessment were selected to guide the analysis and systematically probed in each Member States.

The findings of the assessment are reported in the Assessment Report on National Reference Laboratories in SADC Region document. The first major finding was that there was no uniform definition of the roles, functions and expected standards of national reference laboratories. Existing facilities fell into two broad profiles: diagnostic and public health, in a small number of Member State laboratories were a hybrid of the two major categories.

The profiles dictated the staff complement and equipment, consequently determining the types of services provided. Despite the existence of relatively distinct national reference laboratory models, neither role was performed comprehensively and consistently in a majority of Member States. The capacity to deliver on diagnostic functions was limited even in laboratories with a diagnostic profile. Often times, the scope of public health services delivery was also limited despite the existence of a public health-oriented laboratory. There were diagnostic and public health service delivery gaps.

The most consistent diagnostics gaps were in the provision of new and advanced tests that are essential for patient management. With respect to HIV and AIDS, TB and malaria, there was a limited capacity to provide essential drug sensitivity testing. Only one Member State provided routine HIV drug resistance assays and only one provided routine second-line drug sensitivity testing for TB, the diagnostic method used for the detection of extensively drug-resistant TB (XDR-TB). The capacity to provide specialised malaria diagnosis was also limited to a handful of Member States.

There were also major gaps in the public health component of Laboratory services delivery. In addition to the gaps in diagnostic and public health laboratory service provision, there were inadequacies in the scope and practice of quality assurance and laboratory information management. These negatively affected the capacity of the laboratories to deliver on both those services.

Commonly observed factors that could account for the widespread inadequacies included the absence of policy guidelines detailing the expected roles and functions of the national reference laboratories, the absence or inadequacy of human resources, the unavailability or poor servicing of equipment, and financial resource constraints.

Overall the assessment noted widespread gaps in laboratory service provision in SADC Member States.

The priority intervention recommended by the assessment is the strengthening of national reference laboratories to provide them with the capacity to offer of the required services. It is
also noted that the causes of inadequate capacity are deep-rooted and cannot be addressed within a short timeframe.

Several structural challenges have to be overcome before full national reference laboratory capacity can be realised. The laboratories with a diagnostic profile, were by design not resourced to carry out public health functions. Key personnel, such as epidemiology or surveillance officers, were not part of the laboratory staff complement. There were also limited numbers of Member States with designated posts for laboratory epidemiologists, information technology personnel and laboratory statisticians.

The availability of posts was not the only challenge; most Member States did not have training facilities for these categories of laboratory staff. Information management was further compromised by the limited availability of standardised data collection tools and inadequate operational logistics including the absence of vehicles, and by unreliable telephone communication and the lack of data analysis expertise.

There were no obvious alternative sites from where the essential services were being, or could be provided. The epidemiological disease map of some Member States was therefore reliant on clinical notifications that were not adequately supported by laboratory results. Similarly, public health-type national reference laboratories were not designed to carry out routine diagnostics and these were compromised by factors similar to those seen in diagnostic laboratories.

Human resources availability was restrictive in 12 of 14 Member States. The majority of national reference laboratories were staffed by technical-level personnel, most of who were general diploma holders with no specialised training in specific laboratory departments. The number of laboratory scientists was limited, and only a handful had basic qualifications. The human resource capacity to conduct molecular biology testing was available in five Member States. Even when technical capacity was available, limited financial resources to install the required equipment, and to procure reagents and consumables hampered performance.

The gaps that were observed in the situation analysis were systemic and cannot be bridged in the short term.

A review of policies and the redefining of laboratory mandates, accompanied by adequate financial and human resource support, can in the long term strengthen national reference laboratories and enable them to perform their roles and functions. The diagnostic and public health needs of Member States, however, require attention without delay. Interim service provision arrangements are therefore proposed, pending the strengthening of national reference laboratory capacity.

The proposed solutions are therefore two-fold. They serve to fill the existing gaps, while also addressing the causes of those gaps. They recognise the immediate deficits (which are predominantly in diagnostic service provision) and propose diagnostic supranational reference laboratories as the appropriate response.

These diagnostic supranational reference laboratories should, in the first instance, concentrate on the diagnosis of HIV and AIDS, TB and malaria. The proposed solutions also recognise that permanent, more difficult, answers lie in the strengthening of national reference laboratories.

Public health functions, in particular, are best addressed at the level of Member States and should be augmented by the strengthening of the national reference laboratories. The relevant guidelines have been drafted (Functions and Minimum Standards for National reference Laboratories in SADC Member States, 2009).
Finally, there are intrinsic laboratory functions and roles that are disease-neutral, but which affect all key aspects of laboratory service provision. These include human resources, quality assurance and information management. Neither the national reference laboratories nor diagnostic supranational reference laboratories can address those satisfactorily. The mandate to address this category of services rests with specialised regional centres of excellence.
3. DEFINITION AND SCOPE

A supranational reference laboratory is a laboratory that provides its services beyond national borders. The purpose of such a facility would be to complement in-country deficits in capacity. As such, a supranational reference laboratory should serve as referral facility for national reference laboratories. The supranational entity should perform diagnostics that are technically complex or that require equipment and human resource competencies that are not present in referring Member States. Examples include drug resistance testing for HIV (HIV-DR) or TB (MDR and XDR), and the detection of parasite resistance to malaria medicines.

While supranational reference laboratories provide diagnostic services, the strengthening of national reference laboratories should be delegated to facilities with the requisite capacities. For convenience, those are termed “centres of excellence and expertise”.

Such centres would retain the latitude to address areas of laboratory practice in which they have adequate expertise. They are not disease-oriented, but provide essential complementary functions for service delivery. Their mandate should be to address some of the root causes of current deficits which include non-discipline specific considerations, such as human resource development, specialised training, quality management implementation and the establishment and harmonisation of systems of information collection and its management. Centres of excellence should have superior technical expertise, human and material resources, equipment and appropriate facilities.
4. **JUSTIFICATION**

The proposal to establish supranational laboratories is based on the realisation that gaps exist in laboratory service provision and that these cannot be addressed in the short term. These inadequacies impinge on the realisation of the objectives of the *Maputo Declaration* (2008) and the subsequent WHO African Region Ministerial Meeting in Yaoundé (2008). This limited capacity hinders achievement of the Millennium Development Goals (MDGs) that depend on laboratory service provision.

The proposal is informed by the results of an assessment of the functions of existing national reference laboratories, which noted a variety of inadequacies and observed that these could not be adequately addressed with existing capacity. Among the most urgent aspects were the limited diagnostic capabilities to address the major communicable diseases, HIV and AIDS, TB and malaria.

The capacity to conduct genotypic resistance tests to identify HIV drug resistance was present in three Member States (and was routinely applied in only one of them), leaving at least 12 Member States without national access to those diagnostic capabilities.

With respect to TB, only nine Member States had laboratories with the capacity to diagnose multidrug-resistant (MDR) and only one (South Africa) had the capacity to diagnose extensively drug-resistant (XDR) TB. Five Member States reported cases of XDR-TB. The highest reported number of cases of MDR- and XDR-TB were in countries, which had the diagnostic capacity or the resources to enable referral for diagnosis.

The capacity to diagnose resistance to anti-malaria agents and insecticides was inadequately represented in Member States. These diagnostic services are essential. Their absence in several Member States stems from human, financial and infrastructural resource, and other constraints.

The deficits in diagnostic capacity occur alongside weak public health service provision. The net effect is that the scope of communicable diseases within Member States is not fully appreciated, and when patients present with communicable diseases, the ability to make the required diagnostic tests is limited. There may be silent epidemics, which have a potential to be spread across the region. The urgency to diagnose is high. These considerations are specifically addressed by the call for cooperation and the sharing of expertise as expressed in Article 9 of the *SADC Protocol on Health*. This can be achieved through a twin-track approach that provides:

- Urgent services though the supranational reference laboratories; and
- Opportunities for the strengthening of national reference laboratories through centres of excellence and expertise.
5. PROCESS FOR DEVELOPMENT OF THE MINIMUM STANDARDS

The process for the development of these regional minimum standards was participatory including Member States, the SADC Secretariat and various stakeholders. The process was also informed by internationally-recognised best practices,

Firstly, a desk review of the current national, regional and global policies relevant to reference laboratories was conducted. This was followed by individual country assessments in each Member State, during which key informants within the respective programs, including development partners were consulted to provide information on the state of programmes and policies. The respondents also shed light on some challenges and best practices. Each visit culminated in a country level assessment report which was reviewed and validated by officials from Ministry of Health of each Member State.

The country reports were then compiled to inform a regional picture of the situation and response analysis. The draft regional assessment report was used as a basis for Regional Minimum Standards. Both the draft Regional assessment report and the draft regional minimum standards were then reviewed by a technical team for technical soundness on 7-8 May 2009 at Windhoek, Namibia. The team comprised Member States, Technical Partners and the SADC Secretariat. The purpose of the review team was to strengthen the quality of the documents.

Following the technical review and the incorporation of the comments, the documents were then presented to a regional workshop for validation of the situation and response analysis report and consensus building on the proposed regional minimum standards. All Member States and major stakeholders including regional partners and civil society organisations were invited to the validation and consensus building workshop. The workshop was held on 4-6 August 2009. The meeting recommended the draft reports for approval through the SADC structures subject to the incorporation of suggested changes.

Accordingly, the revised reports were reviewed by the CD Project Steering Committee at their meeting in September 2009 for technical soundness and recommendation for approval by Ministers. Finally, the document was reviewed by Senior Officials in Ministries of Health and those responsible for HIV and AIDS before being submitted for approval by the joint ministerial committee of Ministers of Health and those responsible for HIV and AIDS. The document was approved at the joint meeting of Ministers in November 2009 in Ezulwini, Swaziland.

6. PROPOSED MODELS

The logic and purpose of establishing supranational reference laboratories broadly determines the models that will be followed to address the gaps.

The purpose of the laboratories is primarily to fill existing gaps in service provision, pending the strengthening of relevant capacity in the national reference laboratories.

In cases where the deficits are in diagnosis, diagnostic supranational reference laboratories should provide the required solution. Where gaps are not within the realm of diagnosis, the proposed model would recognise and capitalise on the strengths of existing laboratories, which will then be mandated to share their best practices and collaborate with other Member States. The latter shall serve as centres of excellence in the provision of specified services.
6.1 Supranational reference laboratories

Diagnostic inadequacies were prominent in Member States and required rapid solutions. The options for addressing diagnostic gaps were discussed at length during the consensus-building workshop. These included one laboratory for all diseases and separate laboratories respectively for HIV and AIDS, TB and malaria.

The consensus was that a minimum of three disease-specific supranational reference laboratories was required to address diagnostic requirements for the major three communicable diseases.

The supranational reference laboratories should complement the existing National Institute for Communicable Diseases and the Medical Research Council laboratories, which already provide supranational reference laboratory services at the request of the WHO. The justification for the preference included the fact that it is the current practice of Member States to have disease-specific national reference laboratories and that the option is associated with lower initial financial outlay and would be quicker to operationalise, since human resources and equipment are already available.

The importance of disease-neutral aspects of laboratory services was recognised and there was consensus that these should receive undivided attention and should be provided for in separate centres of excellence.

6.2 Centres of excellence

The gaps in the provision of laboratory services extend beyond the technical diagnosis of disease, and impinge on human resource capacity, quality systems, health and safety, and information management.

While diagnostic supranational reference laboratories address diagnosis, these important areas, if left unattended, will continue to negatively affect laboratory services. In order to achieve more holistic development of laboratory capacity, centres of excellence in general areas of deficit should be identified within SADC Member States, and should be mandated to assist in areas where they excel.

The centres of excellence would not be disease-specific. Their purpose is to address generic aspects of laboratory service provision, which are not currently adequately addressed by Member States’ national reference laboratories, and which cannot be readily discharged by diagnostic supranational reference laboratories. They would capitalise on the existence of unique or exceptional expertise and the capacity to share the same with other Member States. The sharing of technical expertise would be in line with the call made in the SADC Protocol on Health.
7. FUNCTIONS AND MINIMUM STANDARDS

The purpose of the supranational reference laboratory is to complement the deficits in Member States’ national reference laboratories. Supranational reference laboratories would have a wide range of competencies and functions. Their capacity to provide back-up service should therefore be robust.

Some minimum standards need to be outlined in order to address the expectations of the beneficiary national reference laboratories. A diagnostic supranational reference laboratory would be responsible for the advanced testing of samples, and should have the relevant human resource and equipment to offer those services.

Other major areas of deficit include inadequate personnel numbers, quality assurance, information management systems, as well staff health and safety. The supranational reference laboratory should have adequate capacity to address those shortcomings.

This summary of the expected functions and minimum standards is intended as guidance for Member States national reference laboratories that aspire to provide supranational reference laboratory services.

7.1 Diagnostic functions

7.1.1 Confirmatory and specialised testing

National reference laboratories currently perform a limited range of tests. The reasons for this include the costs, the human resources, the technical capacity and the sophistication of the equipment that are required. Tests that were rarely requested, were costly or required advanced technical expertise and sophisticated equipment were not performed in the majority of Member States, even if indicated for the management of patients.

- It is therefore essential, in the interest of patient care, that tests which cannot be performed in Member States’ national reference laboratories should be referred to a supranational reference laboratory. The referral of rare tests to one regional centre would enhance capacity development. This is also an important transitional measure, which allows access to specialised diagnostics while capacity is developed in national reference laboratories. The conduct of specialised testing at supranational reference laboratory has the added advantage of the increased sample numbers that are useful for effective quality control and quality assurance.

7.1.2 Drug resistance testing

Supranational reference laboratories should perform drug sensitivity testing for the Member States whose current capacity does not allow the performance of these tests.

- The performance of genotypic testing to detect HIV-drug resistance, second-line drug sensitivity testing for TB, and the testing of parasite resistance to anti-malaria drugs and insecticides is a priority. This capacity was limited across SADC Member States.

- The availability of this capacity at the supranational reference laboratory should be utilised to facilitate region-wide disease surveillance.
• The laboratory data should be utilised to monitor incident levels of resistance to medicines used in the treatment of HIV and AIDS, TB and malaria.

• Drug resistance data should be used to compile a data bank on patterns of resistance to medicines in the SADC and to prompt coordinated interventions to mitigate the same.

• Data should be analysed periodically and used to identify operational research for health aimed at understanding factors that influence the emergence of hotspots and that can mitigate them before they spread across the region.

7.1.3 Quality assurance

Major challenges in the provision of quality assurance were observed in Member States and across the disciplines. The challenges were systemic.

• The supranational diagnostic reference laboratories should be mandated to assist in the development of quality systems in their respective areas of testing (HIV and AIDS, TB and Malaria).

However, the reporting of quality-assured results by the supranational reference laboratory is unlikely to improve quality management in the referring national reference laboratories.

• There should be parallel systematic efforts to inculcate quality practices at the level of national reference laboratories. The efforts are best spearheaded by currently operational quality assurance schemes, which are better placed to address the quality management systems, rather than concentrate on disease-specific quality assurance and proficiency testing.

7.2 Public health functions of a supranational reference laboratory

7.2.1 Surveillance and epidemic response

Disease surveillance provides the information needed for pre-emptive and corrective health interventions. At a Member State level, the responsibility lies with the national reference laboratory; this role is not reciprocated at a regional level.

• The supranational reference laboratory should be mandated to collaborate with national reference laboratories in consolidating region-wide surveillance data for priority intervention diseases.

• On the basis of such data and with the expert assistance of laboratory epidemiologists and statisticians, the supranational reference laboratory should develop an accurate pattern of the distribution of communicable diseases in the SADC. The information should assist SADC Member States health authorities to coordinate policies in response to possible epidemics.

• The supranational reference laboratory should have the necessary resources to coordinate disease surveillance and provide laboratory leadership in responding to epidemics and other emergencies within SADC.
7.2.2 Information management, monitoring and evaluation

Information is the tool that guides public health implementation and interventions to mitigate communicable diseases. The capacity to gather, analyse and disseminate information was inadequate in many Member States. Challenges included the absence of enabling policies, the shortage of human resources, inadequate financial resources and crippling transport and communication logistics.

- The supranational reference laboratory should assist in the development, harmonisation and standardisation of data collection tools.
- Given the recommendation of the consensus-building workshop that more than one laboratory may be tasked to serve as an supranational reference laboratory, it will be desirable to seek the assistance of SADC experts to standardise data collection tools and harmonise their use in disease surveillance.
- On the basis of such data and with the expert assistance of the laboratory epidemiologists and statisticians, an updated overview of the distribution and changing patterns of disease in the SADC region can be maintained.
- The supranational reference laboratory should serve as an expert focal source of disease-related data and disseminate it timely to allow prompt interventions. The supranational reference laboratory or other centres of excellence should be accessible to national reference laboratories of other Member States.
- The laboratory should be electronically accessible to expedite reporting of results and surveillance communication.

7.2.3 Training, capacity building, skills transfer and operational research in health

National reference laboratories set standards for testing within Member States, and influence the syllabi of training institutions to suit national testing programs at pre- and in-service levels.

- The supranational reference laboratory should facilitate the coordination and harmonisation of the practices across SADC, thus providing training opportunities and mentorship for personnel from Member States. The activities should include continuing professional education.
- Relevant modules (residential or distant) should be designed by specialists in their respective fields.
- Interactive participation should be encouraged and facilitated. Ad-hoc training programs should be conducted by the supranational reference laboratory, and should include training on the use of newly introduced equipment and new techniques.
- The practicalities should include site visits, assistance in setting up specialised laboratory departments (such as TB and HIV), recommending equipment, and training personnel in their use.
7.2.4 Promotion of health and safety practices

The supranational laboratory shall be expected to function as a training site and operate as a model laboratory.

- Staff should observe health and safety precautions especially when they process blood and body fluids, which may be infected with Hepatitis B, Hepatitis C, HIV and other viruses.

- The supranational reference laboratory must be in a position to advise on bio-safety and support the implementation of biosafety measures at national reference laboratories. This role begins with advice on the safe, biosafety-conscious design of laboratory buildings, the recommendations of suitable bio-safety equipment and advice on infection control.

7.2.5 Specimen handling and transportation

In line with its diagnostic functions, the supranational reference laboratory shall be expected to receive and dispatch samples of infectious biological materials to SADC Member States.

- Guidance on packaging and transportation of specimens shall be provided by the relevant SADC coordinating structures, in consultation with WHO.

- Procedures to ensure the safe transportation of samples by commercial carriers shall be put in place. Supranational reference laboratory shall be required to liaise with relevant authorities to the dispatch of samples from the laboratory to other centres, using accredited courier services and in compliance with both local postal regulations and International Air Transport Association (IATA) provisions.

- Independently, it is desirable to harmonise regulations relating to the mailing of biological materials within SADC. This includes the harmonisation of regulations affecting the conduct of couriers, port health authorities and customs offices. This should facilitate the rapid clearing of test samples once they are received.

7.3 Minimum standards for supranational reference laboratories

The mandate of supranational reference laboratories is to provide their services to their national counterparts. The laboratories should, therefore meet certain minimum standards. The basic standards are those of national reference laboratories which have been outlined elsewhere (*Functions and Minimum Standards of National Reference Laboratories in SADC Member States, SADC, 2009*).

- The provision of regional services requires that those basic standards be exceeded. One mechanism for achieving this is to seek accreditation with relevant bodies. (A list of the minimum standards is outlined, and specific requirements pertaining to the major communicable diseases are attached in the annexes.)

- Member States offering to provide a supranational reference laboratory should establish policies or legislative instruments that enable the operation of the laboratory. The policies should be operationalised through agreed strategic implementation plans. The minimum standards are summarised and some details are included in discipline-specific descriptions.
• The human resources required for the provision of these services should be adequate and appropriate. The recommended staff complement is attached (ANNEX I).

• The state of physical infrastructure should be appropriate for the purposes. The design of the laboratory should meet international design standards. A biological safety level 3 would be required for laboratories providing supranational reference laboratory services for TB.

• Equipment essential for the provision of envisaged services should be available. The equipment could be referenced on the recommendations of the *Maputo Consensus Meeting* (2008).

• Robust quality management systems should be in place, and should be modeled on ISO (International Standardization Organization) 15189.

• The supranational reference laboratory should demonstrate the capacity to provide a rapid turnaround time for test samples.

• Health and safety considerations should be addressed to create a safe and conducive working environment. This could be guided by the provisions of ISO (International Standardization Organization) 15190.

• The supranational reference laboratory should be accredited or accreditable by relevant regional or international accreditation bodies.

• The supranational reference laboratory should have the capacity and facilities to adequately deliver on the expected training functions.

• The supranational reference laboratory should ideally have the linguistic capabilities necessary to facilitate communication with Member States' national reference laboratories.
8. ROLES, FUNCTIONS AND MINIMUM STANDARDS FOR REGIONAL CENTRES OF EXCELLENCE

8.1 Roles and functions

Regional centres of excellence are intended to complement and not duplicate the functions of disease-specific supranational reference laboratories. The functions provided are essential, crosscutting and disease neutral.

While the supranational reference laboratory have diagnostic and public health roles, and carry out disease-specific functions, centres of excellence will address the additional areas of critical deficit that were identified in the situation analysis. It was noted, for example, that information management, as well as the numbers and qualifications of laboratory personnel, are inadequate, and that there are major challenges in the provision of quality assurance.

These gaps affect all laboratory disciplines and cannot be addressed exclusively from disease-oriented supranational reference laboratories, even if the capacity existed. Centres of excellence are therefore proposed as additional ways of addressing these fundamental inadequacies.

8.1.1 Human resources capacity development

The ability of laboratories to function is determined by the numbers, qualifications and capabilities of the personnel operating them. The numbers should be adequate, the qualifications appropriate and there should be processes for replacing and increasing numbers as demand escalates, in-service personnel need continuing professional education.

An examination of the generic and disease specific services expected of a supranational reference laboratory shows an increasing requirement for highly qualified and highly specialised, skilled functionaries. There were significant staffing deficits in national reference laboratories, and there were limited numbers of personnel trained in public health aspects of service delivery. In both diagnostic and public health aspects, the deficits were quantitative and qualitative. These gaps compromise national reference laboratory capacity. Deficits were also observed in the provision of continuing professional education, an important avenue for career enhancement for in-service staff.

- Continuing professional education should be structured in ways that can address the increasing sophistication of diagnostic procedures.

Human resource pipelines are not clearly structured and are not always tuned to demands.

- Human resource development is a long-term effort. Dedicated efforts are needed if the functionality of supranational reference laboratories and strengthening of national reference laboratories are to be achieved. This would allow for limited resources to be pooled in supranational reference laboratories, and would create tandem efforts to ensure sustainable and adequate manpower availability in centres that have the capacity to adapt to changing diagnostic demands.

At Member State level, the numbers of laboratory personnel are being boosted by the establishment of training facilities for technicians and technologists. This process is at its infancy.
in the majority of Member States, few of which have the capacity for specialist training of technologists or scientists. Only two or three train pathologists, and the scope of training is limited.

- The long-term development of laboratory capacity demands increased numbers and qualifications of laboratory personnel. This role should be assumed by centres of excellence in human resource development and training.

- The human resource development function of the centre of excellence will be to provide opportunities for graduates of basic laboratory technologist training programs to specialise in their chosen laboratory fields. One or more centres of excellence should provide specialist training opportunities to scientists graduating from universities and technical colleges and polytechnics. Currently the opportunities are limited and a majority of graduates have to travel overseas to obtain Specialist qualifications.

- There is a need for the SADC region to provide specialised post-graduate training in both diagnostic and public health aspects of laboratory services.

- The training of pathologists should be introduced to cover gaps resulting from very limited numbers of chemical pathologists, haematologists, histopathologists, immunologists, microbiologists and virologists.

- Apart from formal training, centres of excellence should provide continuing professional education for in-service personnel from the Member States.

8.1.2 Quality management

Quality management underpins all the functions of laboratories. Quality management was limited in Member States. There was often confusion in the nomenclature and fundamental misunderstandings about the essence of the practice were evident in most Member States.

- The development of quality management systems should start at national reference laboratories and then be cascaded down the diagnostic pyramids.

- While quality assurance and proficiency testing will be available for disciplines that rely on disease-specific supranational reference laboratories, there are inadequate mechanisms for systematically addressing quality management across laboratory systems and across Member States. The mandate of the centre of excellence in quality assurance and proficiency testing will be to strengthen quality systems at national reference laboratory level.

- The establishment and strengthening of quality assurance practices is an essential prerequisite for any functional laboratory system. The role of the centre of excellence on quality management would be to introduce the concepts, guide their implementation at the level of national reference laboratories, and assist the dissemination of quality practices to all levels of the diagnostic pyramids.

- The centre of excellence shall serve as a resource centre for expertise and in the implementation of quality assurance and proficiency testing. It will have a mentoring role for Member States wishing to establish national quality assurance schemes.

- While external quality assurance for tests performed in diagnostic supranational reference laboratories will be coordinated by the supranational reference laboratories,
the implementation of quality management systems should be undertaken by independent, accredited quality assurance schemes.

8.1.3 Information management, surveillance and research

One of the major attractions of the coordination of diagnostic services in the SADC Member States is the possibility of improving disease surveillance across the region. This is consistent with SADC recommendations for increasing cooperation and collaboration between Member States laboratories.

The presence, magnitude and distribution of diseases, in general, and communicable diseases, in particular, are determined on the basis of statistics derived from epidemiological surveillance. The primary sources of the analysed data are entries made by surveillance services, a key component of which is the national reference laboratory. Priority diseases are identified through this method.

The compilation of the data relies on the existence of effective information management – including its collection, analysis, distribution and use by policy implementers. The situation analysis of Member States national reference laboratories noted that this capacity was weak or inadequate. Consequently, a complete picture of disease prevalence is unavailable and programmes to control epidemics either underestimate or overestimate prevalence. Underestimation risks the outbreak of epidemics, overestimation wastes scant resources.

- The centre of excellence for information management, surveillance and research should establish, standardise and harmonise information management systems and procedures in national reference laboratories. This will include the standardisation of test request forms for diseases of public health interest in Member States.

- Such functions should be undertaken in close collaboration with the national reference laboratories and with oversight from a SADC coordinating mechanism.

- The centre of excellence should facilitate the implementation of best practices through structured and targeted training programmes.

- This should be a key focus area in developing laboratory services in general, and in strengthening surveillance.

- The information management centre of excellence should be mandated to utilise information for the epidemiological mapping and research into diseases of public health interest in the SADC region, and to utilise the results to alert policy implementing agencies of any clustering of diseases. This would lead to more rapid identification of trans-border epidemics, and could trigger timely and adequately (regionally) coordinated interventions.

- This is premised on the timely availability of quality and actionable data. The centres should therefore explore and recommend modalities of rapid information sharing between Member States. In this electronic age, it is essential that the services exploit the capabilities of internet communication and telemedicine to expedite information flow within and between Member States.
8.2 Minimum standards for regional centres of excellence

National reference laboratories that provide human resource development, the development of quality management and information management systems should have a competitive advantage over other centres and should be willing to share their best practices with disadvantaged Member States in the spirit of regional collaboration.

The performance of the roles of regional centres of excellence requires the current availability or imminent development of capabilities that exceed those present in other Member States. The areas considered for priority development are manpower development, quality management and information management.

8.2.1 Human resource development, training and skills transfer

The mandate of a centre of excellence for human resource development and training is to complement the efforts of Member States’ national reference laboratories by providing critical human resources and providing training pipelines. The proposed method is through formal training, tutorship and mentoring programmes. The minimum standards include:

- The existence of capacity to deliver on the mandate. Key components of this capacity will include:
  - Adequate numbers of appropriately qualified faculty;
  - Appropriate ranges and scope of training capabilities and expertise, of training personnel, and the capacity to draft training modules and syllabi to suit the needs of the trainees.

- The existence of suitable physical infrastructure for didactic and demonstration activities as appropriate as well as the capacity to accommodate students during their training.

- The logistical and financial capacity to sustain training programs once commenced.

8.2.2 Quality management

The role of regional centres of excellence in quality management is to assume a lead role in the introduction or strengthening of proficiency testing, quality assurance and quality control in Member States that require the service.

- This should be grounded on systematic on- and off-site training that incorporates theoretical and practical aspects.

- Member States serving as regional centres of excellence in quality management should have accredited quality assurance schemes, which should have adequate capacity to roll out their services to Member States’ national reference laboratories.

- This capacity should include adequate numbers of technically competent personnel, with the expertise to provide training in quality management, guide the development of quality practices in different Member States.

- In addition to human resources, regional centres of excellence in quality management should have a permissive legislative environment, command the logistics necessary to dispatch receive and samples of potentially infectious materials. The REC should have the infrastructure to provide envisaged training.
8.2.3 Information management, surveillance and research

Information management is the cornerstone of harmonised surveillance. This has wide-ranging implications for disease control in the SADC Member States. Major gaps were noted in Member States, and these create an opportunity for the introduction of standardised and robust interventions.

- The strengthening of the services should be geared to address national and regional components of information gathering analysis and dissemination. The minimum requirement for offering this service will be the availability of relevant expertise and the capacity to coordinate activities across Member States and language blocks.

- The cost, technical complexity and centrality of this function makes it unlikely that, in the short term that such capacity will be found in any one national reference laboratory. For the time being, it is recommended that the service be hosted in existing units or sub-units within the SADC Secretariat and is then systematically cascaded to the Member States.
9. Implementation Mechanisms For the Regional Minimum standards

The implementation mechanism defines the key stakeholders and their roles in the implementation of the set standards. Furthermore, it provides guidance on how the supranational reference laboratories and regional centres of excellence will be financed. Lastly, it identifies the critical indicators to be monitored to ensure that the framework is fully integrated in the work of the Member States. To this end, this section is intended to map out the critical players and steps to be undertaken to ensure the establishment and implementation of the supranational reference laboratories and regional centres of excellence, including how they will be financed and monitored.

9.1 Stakeholder roles and responsibilities

The successful establishment and operationalization of the supranational reference laboratory and regional centres of excellence requires the involvement of all key stakeholders at both national and regional levels. To this end, it is important to provide an outline on their roles.

9.1.1 Member States

- The SADC Health Ministers will oversee and monitor the operationalization of the this regional initiatives,
- Member States hosting these laboratories and centres shall ensure that the minimum standards are integrated to the annual work plans of their national laboratory system.
- Member States hosting these laboratories and centres shall ensure that the National Laboratory programmes involve various departments in the Ministries of Health (for example, HIV and AIDS, TB, Malaria,) and key stakeholders in the public and private sectors (for example, development partners, and technical UN agencies such as the World Health Organization
- Member States shall identify challenges to implementation of each standard, identify the specific shortcomings that prevent the standards from being met, and identify the barriers and opportunities for each standard.
- Member States shall develop a detailed financial plan and avail resources for supporting the implementation of the harmonised minimum standard.
- Member States will support this regional initiative by assigning necessary resources particularly infrastructure, human resources and finance.
- Member States will create an enabling operational environment by enacting legislation or preparing policies and guidelines that enable the supranational reference laboratory and regional centres of excellence to implement their regional mandates. National-level coordination will be led by organs of the Ministries of Health.
- Member States will lead efforts aimed at mobilising the necessary resources by engaging national, including private sector partners in public-private partnership formats in order to complement laboratory service delivery.
9.1.2 SADC Secretariat

The SADC Secretariat will coordinate the overall implementation and monitoring of these regional initiatives on behalf of the Ministers of Health. Specific responsibilities will include:

- Advocating for the establishment of supranational reference laboratories and
- Facilitating the harmonisation of policy guidelines and protocols for the prevention and control of TB, TB/HIV and MDR- and XDR-TB;
- Facilitating the establishment and maintenance of the minimum required standards for the provision of envisaged services;
- Facilitating the coordination of the utilisation of the supranational reference laboratories as a centre for the collation and dissemination of epidemiological data for the common benefit of all Member States;
- Promoting the usage of these regional facilities by Member States;
- Coordinating partners for resources mobilisation and technical support in the region;

9.1.3 Other stakeholders

- WHO and other UN agencies, together with bilateral donors, development partners, the private sector, and research and teaching institutions will play an important role in the success of the supranational reference laboratories and regional centres of excellence. The roles will vary with the mandates of the agencies. However technical, financial support will be central components of these contributions.
9.2 Financing mechanisms

The operation of supranational laboratories is associated with long-term expenditure. Financial support will be required in the short and long term.

- Short-term funding will be required to:
  - Assist national reference laboratories to achieve the expected diagnostic capacity of supranational reference facilities;
  - Support and position regional centres of excellence to deliver on their mandates; and
  - Enable the SADC Secretariat to implement its harmonisation and coordinating roles.

- Long-term funding will be required to ensure uninterrupted provision of services by both supranational reference laboratories and regional centres of excellence. The financial implications for hosting the supranational reference laboratory include the provision and maintenance of suitable infrastructure and, as a minimum, the fulfillment of the minimum service requirements of national reference laboratories. This will include the maintenance of the services of the laboratory, the recruitment and retention of human resources.

- The financing of the supranational reference laboratory and the centres of excellence shall be shared by hosting and beneficiary institutions.

- The high priority placed by Member States on the provision of these specialised services should be reflected in budgetary commitments. This will ensure sustainability and shield the service from shocks associated with fluctuations and the conditionalities often associated with donor funding.

- Beneficiary Member States will incur the costs of sample processing, as well as the logistics associated with the transportation of the samples, as is the current practice in the area of confirmatory testing and external quality assurance.

- The long-term financing of regional centres of excellence should revolve around cost for services. While there is a provision for initial support from SADC, the long-term costs will be incurred by the hosting Member States.

- Member States shall ensure that areas that need additional financial resources are identified, with the participation of all relevant stakeholders, including UN agencies, donors, development partners, and NGOs.
9.3 Monitoring implementation

9.3.1 Role of Monitoring and Evaluation in Implementation of Minimum Standards

These minimum standards need to be monitored in order to enable both Member States and the SADC region to objectively assess whether Supranational Reference Laboratories (SNRLs) are devolving their roles and at the same time putting in place regionally agreed on minimum standards. Monitoring is an important management tool that helps to identify implementation progress, challenges and bottlenecks that should be addressed for enhanced impacts. Effective monitoring shows programme managers the extent to which SNRLs are making progress in institutionalising the minimum standards and addressing the challenges that may need attention. Thus, results from monitoring implementation of the minimum standards will inform decisions to fine-tune delivery of laboratory services at the regional level.

9.3.2 Monitoring and Evaluation at MS Level

Member States are the beneficiaries of services provided by SNRLs. Thus, at MS level monitoring will focus on whether MS are receiving the following from SNRLs:

- Support mentoring in:
  - Disease information managements system;
  - Surveillance and research capacity;
  - Laboratory and surveillance personnel
- Documenting “Best Practices”
- Receiving test results for specimen sent to SNRL in good time
- Enhancement of quality assurance systems
- Quality of services provided

Thus, monitoring of SNRLs and Regional Centres of Excellence is in terms feedback that is provided by MS. This information will be recorded by MS when they report on the National Reference Laboratories in a separate section. This information will assist both MS and the SADC region to objectively assess whether SNRLs are moving towards realization of regionally agreed laboratory commitments and harmonisation of laboratory services across MS.

Member States will collect this information on an annual basis and prepare an annual report that is part of their report on National Reference Laboratories. The detailed variables on which information will be collected are in a separate document “Framework for monitoring progress in implementation of regional Policies and Frameworks”.

9.3.3 Monitoring and Evaluation at the SADC Regional Level
At the SADC regional level, tracking implementation progress for the minimum standards for SNRLs will focus on issues relevant at that level. Of interest would be to objectively establish progress in institutionalising minimum standards and extent of implementation of agreed on functions. More specifically, at the regional level monitoring will focus on the following areas:

- Strengthening quality assurance systems;
- Strengthening diseases information management systems;
- Establishment of functional referral systems for diseases specimen;
- Monitoring diseases resistance;
- Use of surveillance including dissemination and utilisation
- Identifying priority research areas informed by surveillance data;
- Development and implementation plans to enhance capacity of personnel;
- Accreditation of SNRL;
- Physical infrastructure;
- Availability of requisite equipment;
- Systems of storing and transporting specimen

Specific details on the information to be collected are contained in the "Framework to monitoring implementation of regional Policies and Frameworks" document. This information will be reported by SNRLs every year latest by 30 April to the SADC Secretariat and will assist the region to make informed decisions in terms of mobilizing resources to support strengthening the functioning of SNRLs.

9.3.4 Reporting Mechanisms

Member States will prepare national laboratory reports that include information on SNRLs every year. The reports will be submitted to the SADC Secretariat annually by 30 April. The reports that will be submitted by MS will also describe challenges that MS are experiencing in devolving their functions and implementing Minimum Standards for SNRLs. On the basis MS reports, the SADC Secretariat will compile an annual regional laboratory report that shows progress in the implementation of Minimum Standards for both National Reference Laboratories and SNRLs in the SADC region. The laboratory report will be part of the diseases annual reports (HIV and AIDS, TB and Malaria). Thus, the submission of MS laboratory reports will be in line with submission of national diseases annual reports as detailed in the “SADC Harmonised Surveillance Framework for HIV and AIDS, TB and Malaria”.

The SADC Secretariat will share the report with HIV and AIDS, TB and Malaria managers and Laboratory Experts from SADC MS and partner organisations for their review and comments by end of June annually. MS will share their comments with the SADC Secretariat by mid-July every year after which the report is presented to senior officials from MS Ministries of Health and Ministries responsible for HIV and AIDS for review and recommendation to Ministers of Health and Ministers responsible for HIV and AIDS. The report will then be presented at a joint meeting of Ministers of Health and Ministers responsible for HIV and AIDS that is held once a year further review and approval.
The component of the laboratory report will be analysed to identify implementation challenges and recommend concrete solutions to the identified bottlenecks. Thus, the component of the SNRL will be used for decision making and policy reviews at both the national and regional levels.
ANNEX I: Human resources in a supranational reference laboratory

The human resource complement of supranational reference laboratory is determined by the operations of the facility. Variations in human resource requirements may be influenced by the local availability of expertise and discipline specific activities. Purely diagnostic services should be provided by the best-qualified technical staff. These technical members of staff should be complemented by people with expertise in other areas of work which the laboratory is required to perform. The emphasis must be on establishing a laboratory that is functional and to provide the facility with the requisite human resources.

The core personnel should include:

**Administration**
- Administrator,
- Finance officer,
- Logistics officer,
- Data management officer,
- Administrative assistants (secretaries),
- General workers (cleaners).

**Specialised services: Diagnostic**
- Discipline-specific personnel. Best-qualified specialist laboratory scientific officers to provide leadership in the respective disciplines of clinical chemistry, haematology, histopathology and cytopathology, immunology, microbiology, parasitology and virology:
  - Clinical/medical immunologist for an HIV laboratory,
  - Virologist or medical microbiologist for an HIV laboratory,
  - Clinical/medical microbiologist for a TB laboratory,
  - Parasitologist for malaria supranational reference laboratory.
- Supporting technologists and technicians assigned to the departments,
- Epidemiologist,
- Biostatistician,
- Field workers,
- Animal /insect facility workers.
ANNEX II: Disease-specific functions of supranational research laboratories: HIV and AIDS

An assessment of national reference laboratories for HIV and AIDS in the Member States reported limited access to HIV drug resistance (HIV DR) testing. The factors contributing to this included the high and unaffordable costs of the tests, the costs of procuring and maintaining requisite equipment and the lack of technical expertise required to perform such testing.

These constraints are long term; the development of HIV DR expertise cannot be achieved in a short time frame. The urgent need for the services cannot be delayed until the constraints are addressed. Therefore there is need to access a laboratory service with superior diagnostic capabilities, which can pool financial, human resources, equipment and reagents to provide HIV-DR. This service can be provided by a supranational diagnostic reference laboratory and would be in line with the provisions of the SADC Protocol on Health.

Diagnostic capabilities

The capabilities of supranational reference laboratory should, in general, exceed the standards for a national reference laboratory and complement any gaps that exist in the range of services provided at SADC national reference laboratory levels. With respect to HIV and AIDS, the key diagnostic challenges are:

- The lack of capacity for HIV sequencing and resistance testing;
- Limited access to RNA and DNA polymerase chain reaction for viral load testing;
- Limited access to infant diagnosis of HIV infection;
- The inadequate implementation of quality assurance and proficiency testing for viral load testing, serology and lymphocyte subset enumeration.

In order to fill the gaps, the supranational reference facility should:

- Offer HIV viral sequencing for the detection of drug resistance inducing mutations (HIV drug resistance testing).
- Provide facilities for the detection and quantification of HIV viral copy numbers in test samples (HIV-PCR and HIV-DNA testing) to support national reference laboratories that lack in-house capacity.
- Provide an external quality assurance and proficiency-testing scheme for HIV Serology assays, and provide support in the interpretation of discrepant results.
- Provide HIV-RNA quality assurance and proficiency testing for centres performing these tests, thus obviating or complementing the current practice of sending samples to the Centers for Disease Control in Atlanta, USA.
- Assist the establishment of efficient data collection in Member States’ national reference laboratories.

Public health functions of a supranational HIV reference laboratory

Public health functions are carried out within Member State territories. A supranational reference laboratory would be over-arching and would be responsible for providing services to all Member States. Therefore its public health mandate would be limited to the consolidation of
data obtained by Member States’ national reference laboratories, and disseminating such data to relevant end-users and policy implementers. In addition to the diagnostic service provision, the supranational reference laboratory therefore should:

- Develop, standardise or harmonise tools for laboratory data entry between Member States.
- Pool data to generate an overview of the status of HIV-DR in SADC.
- Utilise the sequencing facilities to enable the differentiation between subtypes and determine relationships between HIV strains, thereby generating new epidemiological information regarding the patterns of HIV-DR and determinants of resistance in the SADC region. The information should guide mitigation interventions.
- Take a leading role in the evaluation for new assays and equipment relevant to the diagnosis and treatment monitoring of HIV and AIDS.
- Identify regionally relevant research questions and coordinate operational research for health relevant to HIV and AIDS.

The expected output will be the collection of accurate data on the prevalence and pattern of HIV-DR in Member States, using standardised tools and quality-assured methods. This will enable an understanding of the patterns of transmission of drug-resistant HIV in the Member States and guide interventions aimed at mitigating the same. Such interventions may be informed by the operational research conducted in conjunction with the supranational reference laboratory.

**Training functions**

- Training, capacity building and knowledge transfer should occur in the areas of specialisation with specific reference to the provision of HIV-DR genotyping services.
- In line with the training and skills transfer role of the supranational reference laboratory, there will be an added responsibility to provide technical assistance to national reference laboratories, as required.
- Mentoring and HIV laboratory capacity building should be provided to national reference laboratories.
- A programme should be designed for progressively increasing capacity in national reference laboratories and decongesting supranational reference laboratories. Skills transfer in HIV-DR may result in the localisation of the extraction and amplification steps of the genotyping process leaving the supranational reference laboratory to do sequencing, for example.

**Equipment requirements**

The supranational reference laboratory should be a state of the art laboratory with a range of all basic equipment. With respect to HIV and AIDS diagnosis and treatment monitoring, an abridged listing of specific pieces of equipment to fulfil the diagnostic, staging and treatment monitoring functions of an HIV supranational reference laboratory should include:

- Biosafety cabinet (Biosafety class II),
- ELISA micro plate washer and reader,
• Western blotting apparatus,
• Flow Cytometer for immunophenotyping with reagents and consumables,
• PCR set up for both DNA and RNA testing with accessories (thermal cycler, reader, washer, extractor), micro-centrifuge, centrifuge,
• Equipment for elution of DBS,
• Basic clinical chemistry analyser,
• Incubator for micro plate ELISA plates,
• Refrigerators,
• Freezers (-70°C),
• Centrifuge,
• Incinerator,
• Haematology analyser,
• Lactate analyser,
• DNA sequencing equipment for amplification, extraction and sequencing of HIV for HIV-DR testing and surveillance,
• Non-diagnostic equipment would include functional information technology and communication capabilities.

Human resource requirements for HIV diagnosis

In addition to administrative and support staff, an HIV diagnosis and treatment monitoring service would require laboratory scientists/technologists specialised in immunology, haematology, serology, clinical chemistry and molecular biology. Senior supervisory personnel (including virologists or microbiologists and immunologists) may be required to coordinate training and research activities.
ANNEX III: Disease-specific functions of supranational research laboratories: Tuberculosis

An assessment of national TB reference Laboratories in 14 SADC Member States noted the lack of capacity for second-line TB drug sensitivity testing. The function was available in only one Member State (South Africa).

Access to first-line drug sensitivity testing was limited due to operational and logistical reasons. First-line drug sensitivity testing was offered in 11 Member States, which used solid and liquid media culture systems. Among national reference laboratories offering first-line drug sensitivity testing, frequent discontinuations of testing were reported. The major challenges with first-line drug sensitivity testing was the attrition and non-retention of human resources. Facilities using liquid media systems were hamstrung by the cost of the equipment and reagents.

Second-line drug sensitivity testing was constrained by a lack technical expertise, costs of the equipment, and space. Additional challenges were the poorly standardised methods of testing for TB infection in paediatric populations and inadequate protocols for the diagnosis of extrapulmonary TB. Consequently, these essential services were not being offered.

The implementation of quality assurance and proficiency testing for drug sensitivity testing and microscopy was weak, with one Member States providing the service for a majority of SADC Member States. The logistics for transporting infectious biological test samples to the one Member State that had the capacity were not streamlined. The workload was high, making it harder to accommodate increasing workloads.

- There is an urgent need to provide structured access to MDR- and XDR-TB testing, and a supranational reference laboratory should provide the services until national reference laboratories have developed national capacity. Such a facility should be able to fill the major gaps that exist in national reference laboratories.

Diagnostic capabilities of a supranational TB reference laboratory

- The supranational reference laboratory should be the centre of excellence for the diagnosis of TB in the SADC and should have the capacity to diagnose drug resistance by any available means.

- The supranational reference laboratory should house advanced techniques, including molecular methods that can identify both *M. Tuberculosis* and non-*M. Tuberculosis* species such as the common *M.bovis* BCG and the rare *M.intracellulare, M.parafinnicum, M.mucogenicum, M.asiaticum, M.heckeshornense, M.kansasi* and *M.lentiflavu, M.abscessus, M.cheloneae* or *M. fortuitum*. All these are acid-fast bacilli on the Z-N stain, and can be confused with *M. Tuberculosis*. The performance of the tests at individual labs would not be cost-effective and the tests would be compromised by varying levels of technical competence, and by quality assurance deficits.

- The results should be used as a source of epidemiological information on disease distribution and continued susceptibility to second-line drugs. The laboratory should conduct operational research and serve as a source of expert technical information to assist in policy generation.

In the light of the gaps, the TB supranational reference laboratory should:
Minimum Standards for Supranational Reference Laboratories in the SADC Region

- Be able to confirm MDR and detect XDR strains of TB, and detect TB in clinical material when national reference laboratories do not have the requisite capacity.
- Be able to provide confirmatory testing of all new diagnoses of drug-resistant strains of TB in the SADC.
- Provide external quality assurance services for first- and second-line drug sensitivity testing for Member States’ national reference laboratories.
- Develop, standardise and roll out protocols for more efficient diagnosis of paediatric and infant TB.
- Evaluate new assays for the detection of TB infection and to determine drug susceptibility.
- Alongside diagnostics and in fulfilment of its general surveillance mandate, determine relatedness between TB strains and obtain, characterise and preserve representative strains of TB for research purposes.
- Put in place adequate intellectual property rights agreements.
- Conduct operational research aimed at improving current diagnostic methods and introducing innovative approaches.

Public health functions of a TB supranational reference laboratory

The supranational reference laboratory should:

- Develop, standardise or harmonise tools for laboratory data entry between Member States.
- Pool data to generate an overview of the status of TB drug susceptibility in the SADC.
- Establish a mechanism of frequently updating and disseminating the epidemiological patterns of MDR- and XDR-TB.
- Establish a compendium of factors that favour the development of MDR- and XDR-TB in order to provide guidance for policy makers.
- Utilise the sequencing facilities to enable the differentiation between subtypes and determine relatedness between TB strains thereby generating of epidemiological information regarding the clustering of MDR- and XDR-TB in the SADC.
- Take a leading role in the evaluation for new assays and equipment relevant to the diagnosis and treatment monitoring of TB.
- Identify areas of operational research and coordinate the same.

Essential equipment

The basic equipment required for the diagnosis of TB is listed below. Additional equipment will be required for second-line drug sensitivity testing.
Equipment required for a TB diagnostic laboratory:

- Autoclaves,
- Biological safety cabinets (BSC Class II with Germicidal UV lighting),
- Level 3 containment facility,
- Light microscopes,
- Fluorescent microscopes,
- LED microscopes,
- Staining and slide drying equipment,
- Reagents and consumables including stains,
- Centrifuges,
- MIGIT liquid culture systems (MGIT manual or MIGT 960),
- -80°C Freezer,
- -20°C Freezer,
- Refrigerators 2 to 8°C,
- Incubators,
- Inspissations,
- PCR Gene Probe assay,
- Weighing scales,
- pH meters or pH indicator strips,
- Water baths liquid nitrogen,
- Ovens,
- Plate counter,
- Water bath,
- Sonicator,
- PCR lab complex and equipment (Amplifier, Thermal Cycler),
- Gel electrophoresis equipment,
- Negative Pressure Laboratory Facilities for TB Culture and DST,
- ELISA reader,
- Micro centrifuge,
- Vortex,
- Disinfectant,
- Paper towels,
- Wash-up.

Training functions

Education, capacity building and skills transfer in the provision of TB diagnosis is a core training function. In line with the training and skills transfer role, the supranational reference laboratory will have the added responsibility to provide technical assistance to national reference laboratories, as required. A TB supranational reference laboratory should offer mentoring and TB laboratory capacity building for national reference laboratories.

Human resources

The TB supranational reference laboratory should be served by general human resource personnel outlined above (administrative, surveillance, biostatisticians, epidemiologists, information technology, logistics and other support staff). Core members of the technical staff should include:

- Departmental or laboratory administrative head with departmental support staff,
- Consultant level microbiologist,
- Molecular biologist,
- Specialist laboratory scientists/technologists (microbiology),
- General laboratory technologists,
- Instrument technician,
- Laboratory assistants.

The numbers will vary with the workload. Additional responsibilities for quality systems management, health and safety and infection control can be assigned to these members.
ANNEX IV: Disease-specific functions of supranational research laboratories: Malaria

Current status of malaria national reference laboratories and gaps

Whereas malaria is a major contributor to morbidity and mortality in the SADC, there are very few designated malaria diagnostic reference laboratories in Member States. Officials could rarely name their referral facilities for malaria diagnosis.

Only two Member States have existing national reference laboratories for malaria. Malaria was more of a public health concern than a diagnostic challenge. Diagnosis was carried out as a component of parasitology units in the tertiary hospital laboratories and the methods used were the same at all laboratory levels. Diagnostic methods are limited to the examination of blood films and rapid immunochromatographic diagnostic tests.

There was active research into malaria in five Member States. The research areas included the validation of rapid diagnostic tests, the use of phytotherapy in malaria, intermittent malaria treatment in pregnancy, and the determination of parasite resistance to anti-malaria medicines. One Member State was piloting the use of polymerase chain reaction as a malaria diagnostic tool.

The key challenges faced by national reference laboratories that need to be addressed by a TB-supranational reference laboratory include:

- A limited range of diagnostic options for malaria in a region where the disease is endemic;
- Limited epidemiological activities relating to the malaria epidemic;
- Limited strategies for sentinel surveillance of disease and delayed responses to emergent resistance with resultant mortality;
- The lack of capacity for the detection of parasite resistance to anti-malarials and insecticides;
- Weak implementation of quality assurance and proficiency testing for drug sensitivity testing, with only one centre providing the service in the SADC region and access to other centres hamstrung by poorly standardised logistics of transporting infectious biological materials.

Malaria diagnosis

A national reference laboratory for malaria diagnosis, while retaining the capacity to perform all malaria testing methods, should provide a specialised diagnostic service, support quality assurance and training, carry out tests to detect drug-resistant mutations of the malaria parasite by molecular tests (including polymerase chain reaction) and identify areas of operational research and coordinate their conduct.

The current basis of malaria diagnosis is the examination of blood film slides and blood samples, using a range of rapid diagnostic tests. The use of molecular techniques including polymerase chain reaction is being piloted. It is hoped that laboratory diagnosis will antedate clinical diagnosis of parasite resistance to current drugs. The tests will include: microscopy, rapid diagnostic testing, and molecular methods (including polymerase chain reaction).
Equipment

The range and sophistication of equipment used for malaria diagnosis is limited. In addition to general laboratory equipment, the malaria laboratory utilises light microscopes and accessories for the staining and drying of slides as well as hand tally counters. Other pieces of relevant equipment include polymerase chain reaction and ELISA systems.

Human resources

The personnel required for a malaria national reference diagnostic service include:

- Administrative head of laboratory/department/unit,
- Parasitologist or microbiologist,
- Molecular biologist,
- Laboratory scientists (microbiology/parasitology),
- Specialist laboratory technologists (malaria),
- Instrument technician,
- Laboratory assistants.

Discipline-specific recommendations: malaria

The diagnostic functions that can be fulfilled by a supranational reference laboratory for malaria are therefore limited to molecular tests and research methods. Therefore the recommendation is to establish a centre of excellence for malaria research, diagnosis and training.

The centre will be expected to have the capacity to diagnose resistant strains, to guide therapy and to conduct epidemiological surveillance studies. This should be complemented with training and skills transfer portfolio.
ANNEX V: General infrastructure and equipment requirements for a supranational reference laboratory

Guidelines for the design and specifications of the physical structure of laboratories have been published by many authorities, including the National Institutes of Health in the USA. These vary according to the levels of biological safety and physical containment required. National reference laboratories for HIV and AIDS, TB and malaria will also vary according to these criteria.

For national-level laboratories, a P3 containment level should be the target. Otherwise, buildings should be designed to have windows that open to the outside and that are fitted with fly screens. Bench tops should be covered with material that is impervious to water, resistant to acid, alkali, organic solvents and moderate heat.

**Physical plant**

There are equipment requirements that are discipline-neutral.

- In the SADC context, the availability of back-up electricity generators and adequate water storage is essential.
- Buildings should be equipped with sinks for hand washing, autoclaves, deionisation/water purification facilities, glassware washing facility, ovens for baking glassware, crushed ice machine and ice buckets and fume hoods.
- The range of refrigeration facilities should include refrigerators, -20°C, -70°C or -80°C freezers and liquid nitrogen storage facilities.

**Equipment**

If cell culture work is envisaged, laminar flow hood, biological safety cabinet (level II), CO₂ incubators, microscopes (including inverted microscopes), high- and low-speed centrifuges, ultracentrifuge and a dark room may be considered.

Depending on the specifications of the national reference laboratory, other equipment should include electrophoresis equipment, water baths, cacuum oven, cacuum pumps, lyophiliser, Spin vac, spectrophotometer, sonicator, pH meter, and calculators. There will be need for access to personal computers and relevant software packages.

Small equipment and the reliable supply of consumables are crucial for the performance of any analyses and for the functioning of the national reference laboratory. This includes mechanical pupating: Pipetman, Gilson or Eppendorf 0-20, 0-200, 0-1000ul with appropriate tips. Autoclaving requires leak-proof autoclave bags. Personal protective clothing should include laboratory coats, NP95, masks and gloves.

Immunophenotyping in an HIV and AIDS laboratory requires a Flow Cytometer and single, dual, three-colour, or four-colour reagents and consumables such as Erythrocyte lysing, fixation and permeabilisation solutions and calibration standards. The major producers of flow cytometry reagents are BD, COULTER and DAKO.