

Key Considerations for Introducing New HIV Point-of-Care Diagnostic Technologies in National Health Systems

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ACRONYMS

AIDS Acquired Immune Deficiency Syndrome

ART antiretroviral therapy

CE Conformité Européenne

CHAI Clinton Health Access Initiative

CDC (U.S.) Centers for Disease Control
and Prevention

EID early infant diagnosis

FDA U.S. Food and Drug Administration

FIND Foundation for Innovative New Diagnostics

HIV Human Immunodeficiency Virus

IVD in vitro diagnostics

ISO International Standards Organization

M&E monitoring and evaluation

POC point of care

PQ Prequalification/Prequalified

RDT rapid diagnostic test

SDGs Sustainable Development Goals

SOP standard operating procedure

TWG technical working group

UNAIDS Joint United Nations Programme on HIV/AIDS

UNICEF United Nations Children's Fund

WHO World Health Organization



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EXECUTIVE SUMMARY

This document describes the key areas that national governments should consider for the introduction and scale-up of point-of-care (POC) diagnostics within national programmes, as new innovative POC technologies are being introduced into the market. The next steps taken to include these new innovations within the broader context of national diagnostic networks of conventional laboratories could influence the achievement of the 2030 Fast Track targets for ending the AIDS epidemic. In this Sustainable Development Goals (SDGs) era, the global HIV/AIDS community is guided by the Joint United Nations Programme on HIV/AIDS (UNAIDS) Fast Track Strategy (2016–2021) and the global targets of 90-90-90. POC diagnostics, when strategically introduced and integrated into national diagnostic networks, may help catalyse changes that improve the way diagnostics and clinical services are delivered. This document distils this understanding based on programmatic and market experiences of introducing POC diagnostics through catalytic investments in POC HIV technologies across numerous countries in sub-Saharan Africa.

This key considerations document is divided into two parts. Part I contextualizes the global HIV diagnostic landscape and the role POC technologies have played and can continue to play in the global effort to end the AIDS epidemic. Part II presents key activities for countries to consider as they introduce and integrate POC diagnostics within national programmes. The document includes references to available global, regional and country guidance materials and resources. In parallel, a number of implementing partners are developing tools and resources to support the introduction and scale-up of POC technologies and programming. An accompanying POC Toolkit, which will contain additional tools and guidance, will be aligned to the modules presented in Part II of this document, and will be available online at <www.childrenandaids.org>. The goal of these tools is to enable national technical working groups in countries to create and refine strong guiding frameworks to support the strategic introduction of POC technologies and to ensure improved access to quality-assured POC diagnostics and stronger national laboratory systems.

INTRODUCTION

Launched in 2014, the ambitious Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 Fast Track targets call for 90 per cent of all people with HIV to know their HIV status, 90 per cent of people diagnosed with HIV to receive antiretroviral therapy (ART) and 90 per cent of those on ART to have a suppressed viral load by 2020. Reaching these targets will require an expansion and strengthening of HIV diagnostic services to both ascertain HIV status for many and to monitor the viral load of those initiated and continuing ART for an even greater number. One strategy for this expansion will be the introduction and scale-up of innovative approaches, including point-of-care (POC) technologies, while strengthening and improving efficiencies in existing conventional laboratory systems and the networks between laboratories and health facilities. POC testing may enable more clients to access the benefits of diagnostics, while also facilitating receipt of their results during the same visit. This faster turnaround of results may allow for speedier clinical decisions (e.g., treatment initiation, treatment regimen switch, adherence and counselling, linkage to preventive services for HIV-negative patients, etc.), improved retention in care, and decreased loss to follow-up.

While many considerations for planning and implementing POC testing are similar to those for laboratory-based diagnostic testing, POC testing involves unique challenges when it comes to product selection and placement, training and supervision, device monitoring, service and maintenance, safety and waste management, data management, clinic and patient pathways performance, quality assurance, and supply chain management.

This document provides up-to-date information (as of October 2017) to support the introduction and scale-up of HIV POC technologies, and to guide discussions at the national and subnational levels.

This document is divided into two parts. Part I provides background information on HIV POC testing and its potential contribution to meeting the 90-90-90 Fast Track targets. Part II outlines the steps for introducing HIV POC technologies, including: policy and framework development; strategy and planning; regulations; quality assurance and data management; procurement and supply chain management; implementation; and monitoring and evaluation (M&E). It is important to note that the modules in this document are not intended to serve as a formal guidance or set pattern that favours a given technology or solution. Instead, the modules should be viewed as a set of considerations that countries and national technical working groups (TWGs) can and should tailor for national objectives on a case-by-case basis.



ABOUT THIS DOCUMENT

Audience: This document is intended primarily for country programme managers. Other stakeholders including donors, policymakers, implementing partners, procurement and logistics personnel, and training and quality assurance personnel may also find this document useful.

Purpose: To understand the rationale for as well as the availability and functionality of new POC technologies, and the steps to plan for implementation.

Scope: This document focuses on POC testing as it relates to HIV diagnosis infant virological testing (including early infant diagnosis (EID)), CD4 staging and monitoring, and viral load monitoring.

PART 1



1. RATIONALE FOR THE SCALE-UP OF TESTING

1.1 GAPS IN TESTING ARE WIDESPREAD

Determining the HIV status in people of unknown status and achieving viral load suppression in people living with HIV is the gateway to HIV prevention and improving HIV outcomes. In 2016, 19.5 million of 36.7 million people globally living with HIV were receiving ART, confirming the success of the scale-up of HIV testing and treatment services over the past decade.¹ Still, large gaps in testing, care and treatment remain. More than 14.5 million people living with HIV do not know their status, and only approximately 50 per cent of all HIV-positive people are receiving treatment – leaving 3.8 million people aware of their HIV status and not on treatment. It is estimated that global viral suppression of those people living with HIV is 38 per cent [35–41 per cent].²

In resource-limited settings, too many people never receive care after learning their HIV status, due to inadequate linkages between testing and care services. Access to viral load testing remains low in low- and middle-income countries, despite evidence that this technology supports clinical decision making and can help support the implementation of differentiated models of care.³ The diagnostic situation is still worse for infants who rely on nucleic acid testing for early infant diagnosis (EID)⁴ – with less than 51 per cent getting an EID test by 2 months of age, and of these only 57 per cent receiving their results.⁵ Without prompt initiation of treatment, approximately half of HIV-infected infants will die before their second birthday.⁶ For young HIV-exposed infants in particular, it is critical that we close the diagnostics gap.⁷

Meeting the ambitious UNAIDS 90-90-90 Fast Track targets⁸ will require a significant scale-up of patient identification and diagnostic testing services, as well as a renewed focus on strengthening linkages to treatment and care to ensure that HIV-infected people are initiated onto ART as soon as possible and monitored to achieve viral suppression. The first 90, the diagnosis of HIV, is essential to the second 90, the initiation of ART among people living with HIV. Moreover, in order to improve client outcomes and prevent HIV transmission, viral load monitoring and viral load suppression among people on ART is essential for the third 90. Decentralized diagnostic services, bringing them closer to the population in need, through POC technologies may be one key element in achieving the 90-90-90 Fast Track targets. Importantly, the World Health Organization (WHO) provides clear guidance and specific recommendations to support national governments to scale up infant virological testing and viral load testing for all populations as the global community works together to end the AIDS epidemic by 2030 (see Table 1 to the right).

TABLE 1 WHO recommended testing strategy for infant virological testing and viral load monitoring for all populations

INFANT VIROLOGICAL TESTING		VIRAL LOAD MONITORING	
Age	Recommended testing	Baseline	No viral load monitoring
Birth	Virological testing (conditional recommendation)	6 months after treatment initiation	Viral load testing*
4–6 weeks		12 months* after treatment initiation	Viral load testing*
9 months	Serology testing; if HIV-positive then virological testing	Every 12* months thereafter	Viral load testing*
18 months	Serology testing		

* If viral load is above 1,000 copies/ml, reinforce adherence regimen and repeat after three months; if the virus remains detectable, consider changing to second or third line therapies as per national guidelines.

Source: World Health Organization, *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach*, 2nd ed., WHO, Geneva, 2016.

1.2 LABORATORY-BASED TECHNOLOGIES

The current global market for HIV in vitro diagnostics (IVDs) does not meet the needs of the 36.7 million people living with HIV. Although HIV rapid diagnostics tests (RDTs) for adults and children older than 18 months are widely available and simple to use, access to EID/infant virological testing and viral load monitoring has been more limited due to reliance on complex laboratory-based IVDs. These IVDs require sophisticated laboratory infrastructure and highly trained laboratory technicians that are often only available in larger centralized laboratory settings. As a result, specimens and results must be transported to and from these centralized laboratories. When laboratory systems are not optimized, delays arise throughout the cascade from specimen transport and laboratory testing to the return of results to the clinic, as well as from the clinic to patients, and subsequent treatment initiation. These delays can result in long turnaround times for test results, high rates of patient loss to follow-up and delayed treatment decisions.⁹



2. POINT-OF-CARE TECHNOLOGIES AS A TOOL FOR TESTING SCALE-UP

POC testing is when patients are tested on-site at a health facility and receive their results during the same visit or day. Technologies for 'near point-of-care' testing may require some laboratory infrastructure where electricity is consistently accessible, and therefore cannot currently be operated in primary health-care settings with no electricity.¹⁰ Importantly, testing at point-of-care (and some near point-of-care) brings test results

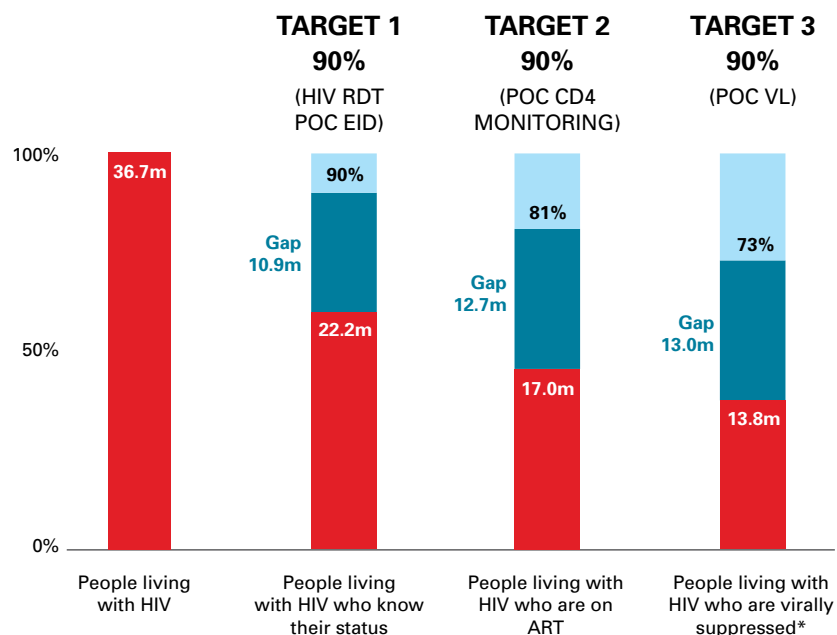
closer to the patient, providing easy-to-use products that do not require constant electricity, refrigeration, sophisticated laboratory infrastructure, or highly skilled human resources. Table 2 on page 13 summarizes the various benefits and challenges related to point-of-care and, to a lesser and varying extent, for near POC IVDs, as compared with conventional laboratory systems.

TABLE 2

Summary of benefits and challenges related to point-of-care and near point-of-care technologies as compared with conventional laboratory network systems

	BENEFITS	CHALLENGES/LIMITATIONS
ACCESS	<ul style="list-style-type: none"> • Results are produced at/near the site of patient care. • Faster turnaround time, even same-day results, allow for immediate clinical decisions, and same-day initiation of treatment, if indicated. • Shorter turnaround time for results reduces the likelihood of loss to follow-up. 	<ul style="list-style-type: none"> • Patient wait times in the clinic, while the results are being generated, may be too long. • Clinic or patient flow may need to be adjusted or revised to provide same-day results. • It may not necessarily result in improved health outcomes, particularly for viral load and if a patient is not linked to care and treatment.
EFFICIENCY	<ul style="list-style-type: none"> • Most infant virological and viral load POC IVDs can run approximately 8–20 tests per day, per instrument.¹¹ 	<ul style="list-style-type: none"> • The throughput of POC and some near POC devices is lower than throughput at the central level (at the central level one person can run 100 or more specimens per day). • If volume is high, more than one POC device may be needed to process the test volume, increasing the cost per test, if all devices are not used to capacity. If volume is low, cost per test may be higher due to lower utilization. • Near POC devices require constant electricity and both POC and near POC devices require some degree of temperature control for operation and storage of reagents (cartridges).
COST	<ul style="list-style-type: none"> • An increased proportion of test results are returned to patients, with less wastage from repeated testing of patients who never receive their test results. • Prices of IVDs (instruments and test cartridges) are expected to decrease over time, except for current IVDs for infant virological testing. 	<ul style="list-style-type: none"> • Making POC cost-effective in low volume areas is currently challenging. • Cost per test run is currently higher than conventional testing (the cost per result received could become comparable to and even lower than conventional laboratory-based testing, depending on the type of device used, the type of test run, and where the device is placed).
OPERABILITY	<ul style="list-style-type: none"> • POC devices can be operated by non-laboratory trained personnel. • POC devices require fewer procedural steps and commodities. • Some reagents and controls do not require refrigeration and have a shelf life of approximately 9 to 12 months, with efforts under way to extend shelf life. • Some devices use low specimen volumes, which are easier to collect. • Most POC devices have built-in quality controls. • Many devices use capillary whole blood; therefore, phlebotomy and specimen processing are not required (except for current near POC technologies for viral load). 	<ul style="list-style-type: none"> • Turnover of operators at health-facility level may be high especially in remote or hard-to-reach areas, making quality testing by trained operators hard to sustain. • As may be already an issue within the conventional lab systems, POC devices will require reagent storage and inventory management, and some facilities (i.e., primary health-care clinics) may not have the requisite space, refrigeration or systems to support POC.
INFRASTRUCTURE	<ul style="list-style-type: none"> • Tests can be performed in wider a range of sites with fewer infrastructure requirements. • Most POC devices are portable, and operable without constant electricity or need for air conditioning. • In remote and hard-to-reach sites where turnaround times for test results may be long, POC devices minimize reliance on specimen referral systems and/or centralized testing facilities. 	<ul style="list-style-type: none"> • As with changes to conventional laboratory technologies, additional training is required. • Supervision and quality assurance may be more difficult due to a greater number of and more dispersed sites. • Near POC devices require constant electricity, computer interface and some degree of temperature control for operation and storage (cartridges).

FIGURE 1 Point-of-care can help address each component in the UNAIDS 90-90-90 Fast Track targets



Adopted from Global Progress report 2016 based on Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS) and UNAIDS/WHO estimates.
* HIV-1 RNA <1000 copies/ml

As illustrated in Figure 1, progress towards the *'first 90'* will be supported by facilitating expanded access to RDTs and infant virological testing in maternal, neonatal and child health clinics and through other child health delivery points, such as pediatric wards and nutrition clinics. Progress towards the *'second 90'* will be supported by effectively linking people to HIV treatment services soon after diagnosis. In settings where universal treatment is not yet possible, POC CD4 testing can continue to support prioritization decisions regarding ART initiation and prophylaxis for opportunistic infections. Finally, viral load monitoring will facilitate progress towards the *'third 90'* by measuring viral suppression. Table 3 to the right describes the different HIV IVDs and their intended use.

TABLE 3 Description of HIV in vitro diagnostics*

TYPE OF ASSAY	DESCRIPTION
INFANT VIROLOGICAL TESTING	An assay that measures the presence of the HIV virus using venous or capillary whole blood or plasma. In order to determine the HIV status of HIV-exposed infants, virological testing is necessary. An immunoassay for detection of HIV antibodies in infants and children younger than 18 months may detect maternal antibodies passively transferred from the mother in addition to antibodies produced by the infant, and therefore may lead to false reactive test results. While an immunoassay can rule out infection, it cannot definitively establish an HIV infection. HIV status in children younger than 18 months must be determined using virological testing. In peripheral facilities with no laboratory capacity, dried blood spot specimens are generally sent to a central testing laboratory for analysis.
CD4 CELL COUNT	A test that measures the number of CD4 cells in venous or capillary whole blood. It is an important indicator for how well a person's immune system is working and to monitor disease progression. With conventional testing, freshly collected whole blood is sent to a laboratory for analysis. With its 2016 consolidated guidelines, WHO recommends a 'treat all' approach. However, if 'treat all' cannot be fully implemented, WHO recommends that CD4 testing be used to prioritize patients. In addition, CD4 testing at the point-of-care can be used for patient monitoring if viral load testing is not routinely available.
VIRAL LOAD	An assay that measures the number of HIV virus copies in a millilitre of whole blood or plasma. This assay helps provide information on how well treatment is controlling the virus or how adherent patients may be, and can help determine whether patients need to switch their drug regimen or require adherence counselling. With conventional testing, venous whole blood, plasma or dried blood spot specimens are sent to a laboratory for analysis.

* See Table 1 for the latest EID and viral load testing strategy as per WHO guidelines

2.1 ACHIEVING THE 'FIRST 90': EARLY INFANT DIAGNOSIS

In order to reach the UNAIDS 90-90-90 Fast Track targets, HIV testing services need to be strategically expanded to diagnose as many people with HIV as early as possible. This includes diagnosis of infants, adolescents and adults. This document is focused on new POC technologies for HIV diagnosis of infants (early infant diagnosis). Adolescent and adult HIV testing is covered extensively elsewhere.¹²

Challenge: Although fewer children are acquiring HIV due to scaled-up efforts to prevent mother-to-child transmission, new infections still occur. About 150,000 new infections among children occurred in 2015,¹³ and a substantial number of these new infections remain undiagnosed due to a number of reasons, including lack of access to HIV testing services for infants, poor retention of the mother-infant pair post-delivery and

poor retesting of the infant/child in the breastfeeding period. Vertical transmission from mother to child can occur during pregnancy, labor and delivery and throughout the breastfeeding period, so HIV-exposed infants must be retested periodically throughout this exposure period.

How may POC help? Testing infants at the point of care with same-day results or significantly improved turnaround time may help ensure that HIV-exposed infants are tested, diagnosed and quickly linked to life-saving treatment services. Birth testing, retesting at regular intervals throughout the exposure period (as per WHO guidelines) and expanding testing services beyond traditional prevention of mother-to-child transmission, antenatal and post-natal services to additional entry points (e.g., inpatient wards, nutrition clinics, immunization and outpatient settings, etc.) may help promote increased testing of HIV-exposed infants and children.

TABLE 4 First 90: Early infant diagnosis

WHO RECOMMENDATIONS ON TESTING INFANTS AND CHILDREN AND ART INITIATION	POC RELEVANCE
<ul style="list-style-type: none"> • See Table 1 for recommended timing for testing of infants and children • In generalized epidemic settings, infants and children with unknown HIV status who are admitted for inpatient care or attending malnutrition clinics should be routinely tested for HIV (strong recommendation, low-quality evidence). • In generalized epidemic settings, infants and children with unknown HIV status should be offered HIV testing in outpatient or immunization clinics (conditional recommendation, low-quality evidence). • ART should be initiated in all children infected with HIV regardless of WHO clinical stage or CD4 cell count. 	<ul style="list-style-type: none"> • Virological testing at the point of care is expected to improve access to results and, if found positive, could decrease time to initiation of treatment. • Where feasible, same-day HIV testing at the time of birth may improve early linkage to treatment, thereby avoiding the early peak mortality at 2–3 months of age in HIV-infected infants.¹⁴

Source: World Health Organization, *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach*, 2nd ed., WHO, Geneva, 2016.

2.2 ACHIEVING THE ‘SECOND 90’: CD4 TESTING

Challenge: Although many countries are moving to treatment for all, as per the 2016 WHO consolidated guidelines,¹⁵ in some countries, after patients receive a diagnosis of HIV infection, eligibility for ART initiation continues to be determined by CD4 cell count. CD4 testing is also valuable for the management of opportunistic infections. Regardless, only 46 per cent of eligible adults were on treatment in 2015, suggesting significant barriers to enrolment. With conventional testing, whole blood samples are sent to a central or regional laboratory for analysis and patients have to return to the clinic on another date to receive their test results and to initiate ART if found eligible. Conventional machines for CD4 diagnostics are expensive and require sophisticated laboratory infrastructure and trained technicians. For the patient, getting a CD4 test result often means repeated visits to the health facility, leading to delays in initiation of ART (*see, for example, Box 1 below*). Unfortunately, many patients are ‘lost’ during this multi-step process. The 90-90-90 Fast Track targets highlight the importance of simplifying this process.

How may POC help? POC CD4 tests at HIV diagnosis help improve patient management by accelerating linkage to care and initiation of treatment in settings where CD4 is still indicated. This is particularly important during late presentation for HIV care – i.e., people with symptoms of advanced HIV disease and who are at high risk of opportunistic infections. Such late presentation remains common in sub-Saharan Africa and other resource-limited settings.

TABLE 5 First 90: Early infant diagnosis

WHO RECOMMENDATIONS ON CD4 TESTING AND ART INITIATION	POC RELEVANCE
<ul style="list-style-type: none"> • CD4 cell count for ART monitoring should be stopped only in settings where viral load monitoring can be assured. CD4 measurement still has an important role to play in assessing baseline risk of disease progression, making decisions regarding starting and stopping prophylaxis for opportunistic infections, and prioritization decisions regarding ART initiation in settings where universal treatment is not possible. • CD4 cell count testing at the point of care can be used to prioritize patients with severe or advanced HIV clinical disease for urgent linkage to care and ART initiation in settings not using ‘treat all’. • If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure. 	<ul style="list-style-type: none"> • Same-day POC CD4 tests at HIV diagnosis allows for immediate decision making, patient management and referral, and improving ART initiation. • Same-day POC CD4 testing can be used to triage sick clients for opportunistic infection prophylaxis.

Source: World Health Organization, *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach*, 2nd ed., WHO, Geneva, 2016.

BOX 1 A patient’s view of POC in Ethiopia

At the Modjo health clinic in central Ethiopia, Sisay Dinku offers counselling to HIV-positive women. The 33-year-old learned she was HIV-positive more than ten years ago. Dinku says things have changed considerably for people living with HIV in Ethiopia.

“There have been a lot of improvements. When I first knew I was HIV-positive, we used to go to the hospitals far away because the services weren’t given at the community centres like they are now,” Dinku says. She also notes the reduction in waiting times for people receiving their CD4 count results. “When I used to get tested I would have to wait one or two weeks for the test results to return. Sometimes you didn’t get results at all, because samples would get mixed on the way there.”

A new device providing same-day CD4 test results has helped cut waiting times for patients at the clinic. The CD4 test machines analyse blood samples and print reports for nurses in 20 minutes, meaning patients can get their

results on the same day as the test is taken. If the results indicate HIV treatment eligibility, patients can initiate treatment immediately.

Dinku says improvements in HIV diagnostics have made a significant difference in patients’ lives, particularly for linking HIV-positive pregnant women to treatment and helping them stay alive. “Let me give you an example,” she says. “When I found out I was HIV-positive, there were eight other people that day who found out too, but I’m the only one that’s alive and survived. The rest of them died because they did not have the support and they could not wait for weeks for test results and have to travel back to the clinic again. They got tense, they got worried, and sometimes they quit from the overall treatment. That’s the result of waiting.”

Adapted from: <www.theguardian.com/global-development/2015/jun/18/ethiopia-hiv-mother-child-transmission-antiretroviral-treatment>.

2.3 ACHIEVING THE 'THIRD 90': VIRAL LOAD TESTING

Challenge: As the HIV virus reproduces within the body, the VL initially increases and then typically reaches a steady set point, if left untreated. The goal of ART is to suppress this reproduction and keep the viral load low to reduce destruction of the body's ability to fight illnesses/progression of HIV disease, as well as the risk of passing the virus to someone else. WHO recommends viral load testing as the *preferred monitoring approach* to detect antiretroviral treatment failure. Measuring viral load can also serve as a proxy for assessing the risk of transmission, as people with high viral load¹⁷ are more likely to transmit the virus. Data reported by 86 countries show that only 38 per cent of people living with HIV had a suppressed viral load in 2015.¹⁸ The faster a person living with HIV is diagnosed and initiated on treatment, the quicker his or her viral load can be reduced to levels that minimize or eliminate the risk of onward transmission. While efforts continue to increase access to viral load testing in resource-poor settings, conventional viral load testing has only been possible in centralized laboratories using large laboratory-based equipment. Some countries have delayed establishing viral load testing programmes due to the complexity of setting up the systems and cost of implementation. Instead, they continue to use CD4 or clinical signs for ART monitoring, despite the new WHO recommendation and evidence of poor sensitivity. However, the demand for viral load testing is expected to grow sharply in the coming years as countries adopt the WHO recommendations.

How may POC help? POC viral load devices at peripheral health-care facilities could increase the uptake of viral load testing and offer same-day results, enabling better treatment monitoring, differentiated care, faster initiation of adherence counselling interventions and/or faster switching to second-line treatment regimens when needed – all of which can help inform the development of targeted programmatic interventions. It is important to note that the impact of POC viral load technologies on patient outcomes was still under evaluation as of December 2017.



TABLE 6 Third 90: Viral load testing

WHO RECOMMENDATIONS ON VIRAL LOAD TESTING AND ART INITIATION	POC RELEVANCE
<ul style="list-style-type: none"> • Viral load is recommended as the preferred treatment monitoring approach to detect ART failure. • Routine viral load monitoring should be carried out at 6 months, 12 months, and then every 12 months post-initiation of treatment if the patient is stable on ART. 	<ul style="list-style-type: none"> • Same-day POC viral up may allow for speedy decision making and patient care and management by allowing for faster adherence counselling and/or switching to second line.

Source: World Health Organization, *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach*, 2nd ed., WHO, Geneva, 2016.

3. EXPANDING ACCESS THROUGH STRATEGIC DECENTRALIZED TESTING

3.1 POC IN THE CONTEXT OF THE TIERED LABORATORY NETWORK

Reaching people with testing services and quickly delivering test results requires reliable and efficient laboratory services. Figure 2 shows how HIV testing services are typically provided as part of a tiered testing service. Each level provides different diagnostic services, tailored to the needs of the setting and according to the capacity of the facility (e.g., infrastructure, staff capacity). For example, at the national level (level 4), services may be targeted towards disease surveillance, validation of algorithms and national data, product evaluation, post-market surveillance, training and supervision, and quality assurance. National and regional/provincial laboratories generally have the capacity to perform high-throughput, laboratory-based nucleic acid testing. In contrast, the capacity of laboratories at district (level 2) and primary care (level 1) facilities is typically limited to serological testing (e.g., RDTs) such that they refer specimens to levels 3 and 4 for virological testing. Community and outreach services (level 0) focus on disease detection by using simpler diagnostic tools such as RDTs.

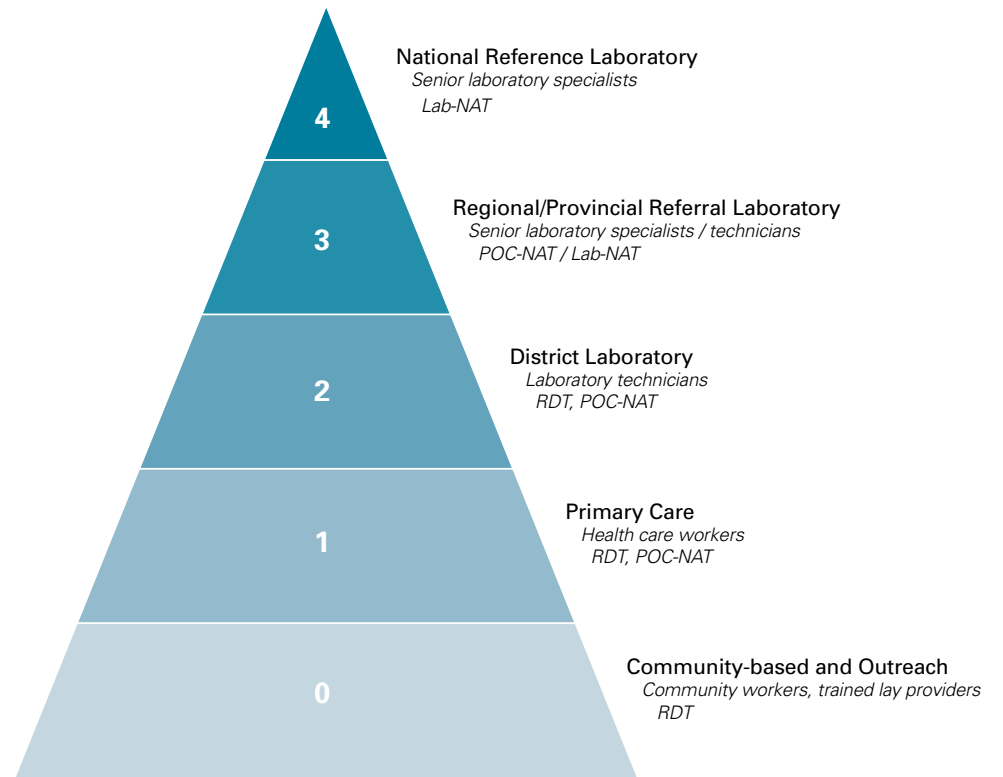
A tiered, integrated laboratory network is fundamental to ensuring accessibility and equity in the health-care system.

POC and near POC IVDs can be integrated at different levels of this network to increase patient coverage and access to testing. To achieve maximum efficiency and coverage, the optimal balance between the five tiers will depend on a range of factors, including geography, populations served, disease profiles, available technologies, capacity, etc. There is no 'one size fits all' approach and POC testing should be introduced to complement and improve existing national testing networks.





FIGURE 2 Tiered laboratory network



Source: Adapted from World Health Organization, *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach*, 2nd ed., WHO, Geneva, 2016.

Note: Lab-NAT: laboratory-based nucleic acid testing; POC-NAT: point-of-care nucleic acid testing; RDT: rapid diagnostic test.

3.2 CENTRALIZED AND DECENTRALIZED TESTING SERVICES

The goal of POC testing is to expand access to high-quality testing services in both decentralized and centralized settings. Laboratory-based testing will continue to play a critical role in providing services in larger hospitals with high patient numbers and as referral sites for decentralized service delivery points. The addition of POC diagnostics could improve the efficiencies of patient flow, particularly in settings with large volumes. However, in settings where people who require HIV testing and monitoring for ART are widely dispersed, it may be necessary to provide testing at the health facility. In those settings, reaching the number of people who require HIV testing and care will require decentralizing diagnostic services to lower levels of care, particularly those that serve high volumes.

With centralized systems, specimens are sent to central laboratories for analysis. Conventional diagnostic technologies require sophisticated laboratory infrastructure, stable electricity supply and highly trained technicians. Because of these requirements, such laboratory equipment is usually located in urban and semi-urban settings. Some countries have a strong sample transport system (*see Uganda example in Box 2*). In those settings, there may be less of a need for decentralized testing services. While there may be reduced turnaround time in settings with reliable transport systems, placement of POC diagnostics could help prioritize patients who present with advanced disease and need speedy diagnostics or viral load testing.

In settings without an established sample transport system, with high volume and/or high loss to follow-up, decentralized testing services to lower-tiered facilities may be the answer to reducing turnaround time for results and increasing retention. Proper placement of POC technologies may also assist in reducing turnaround time and loss to follow-up while the laboratory system is strengthened. An observational study conducted in four primary health-care clinics in Mozambique found that the proportion of patients lost to follow-up before the completion of CD4 staging dropped from 57 per cent to 21 per cent with the introduction of POC CD4 testing, and the total loss to follow-up before initiation of antiretroviral treatment decreased from 64 per cent to 33 per cent.¹⁹

As illustrated in both Mozambique and Uganda, both centralized and decentralized models of testing can be effective in reducing turnaround time for results, and, in the Mozambique example, reducing loss-to-follow up. It is for countries to decide which approach or combination of approaches is most appropriate for their setting. Regardless of which approach is chosen, shorter turnaround time for identification of HIV needs to be closely linked to treatment in order to attain the greatest impact on lives.

BOX 2 A centralized approach to diagnostic services: The case of Uganda

Uganda uses one laboratory, the Central Public Health Laboratory (CPHL), supported by a national specimen hub transport system, to scale up infant virological testing and viral load testing in the country. A hub is a hospital laboratory that provides diagnostic services to lower-level facilities and serves as a conduit for the central laboratory. In Uganda, 100 hubs support 2,550 facilities nationally. A motorcycle rider travels between hubs and facilities, collecting specimens and returning results to facilities daily. With this system introduced, turnaround time for infant virological testing decreased from an average of 69 days before the hub system to 14 days, while turnaround time for viral load testing decreased from an average of 90 days to 28 days in the first year of operation.

Source: Kiyaga, Charles, K. Callaha and S. Phanitsiri, 'Measuring the Impact and Cost of Uganda's Specimen Hub Transport System', Late Breaker Oral Session at ASLM, Maximizing Public Health Impact through Diagnosis and Use, 6 December 2017.

4. POINT-OF-CARE TECHNOLOGY LANDSCAPE



Anecdotally, advocacy efforts in recent years have made the case for HIV POC technologies, resulting in greater political buy-in and increased demand for services. Despite these efforts, new technologies still face market entry barriers that stem from a lack of understanding of market potential, forecasting and investments, regulatory requirements, post-market support and supply chain limitations.

Despite these challenges, opportunities to learn from the scientific evidence and build on country successes exist. Applying lessons learned from HIV antibody RDTs and other earlier HIV POC technologies to create standard processes for POC implementation and scale-up will ease the path for future technologies. However, it must be noted that policies change and, as a result, implementation and scale-up processes will require continuous review.

For additional information on WHO prequalified in vitro diagnostics products, see: <www.who.int/diagnostics_laboratory/evaluations/PQ_list/en/>.

The *Unitaid HIV/AIDS Diagnostics Technology²⁰ Landscape* document provides a comprehensive biannual update on the status of new POC technologies.

PART 2



5. KEY CONSIDERATIONS FOR INTRODUCING HIV POC TECHNOLOGIES

This section outlines key considerations for introducing HIV POC technologies into national health and laboratory systems. It is divided into seven major modules: six distinct (policy and framework development; strategy and planning; regulations; quality assurance and data management; procurement and supply chain management), and one cross-cutting (monitoring, evaluating, and improving quality). Each area consists of multiple sub-areas or components (see Figure 3 on page 24).

These seven modules represent the key areas that should be considered when introducing HIV POC technologies in any country context. Many activities can be undertaken simultaneously across the respective modules, although within given modules some activities are consecutive. The order in which activities are presented here is not meant to be prescriptive, and not all activities necessarily need to be implemented in all countries. These activities are suggestive and countries should adapt and modify according to their country needs and context.

In addition, it is important to emphasize that POC technologies cannot and are not intended to replace conventional laboratory-based testing. Rather they are meant to complement and extend the reach of testing where service delivery gaps have been identified. Strong conventional laboratory programmes are an essential component of a resilient health systems and the backbone on which to build POC testing.

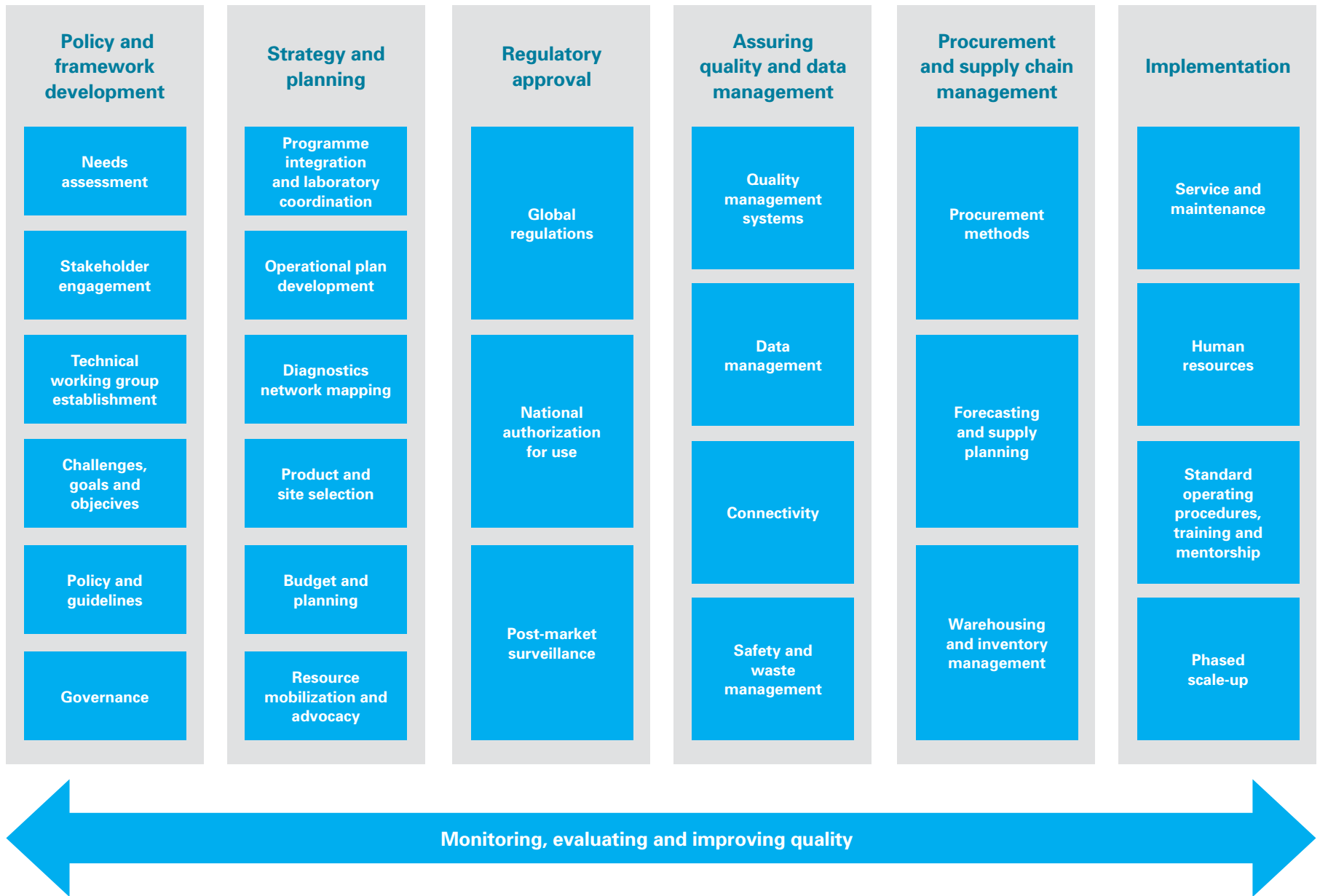
5.1 POLICY AND FRAMEWORK DEVELOPMENT

National commitment to the introduction and roll-out of HIV POC technologies as demonstrated through a needs assessment, stakeholder engagement and consultation, the development of functional and effective TWGs, and relevant POC policy development is critical to the successful adoption and roll-out of POC technologies.

TABLE 7 Policy and framework development

DOMAIN	SUMMARY OF RECOMMENDED ACTIVITIES
Needs assessment	<ul style="list-style-type: none"> Analyse national- and facility-level data relevant to introducing POC diagnostics. Assess the enabling environment for introducing POC technologies in the existing laboratory and health systems (e.g., policy, regulatory frameworks, etc.). Consider the operational requirements for scaling up POC as well as funds and resources available for scale-up.
Stakeholder engagement	<ul style="list-style-type: none"> Identify and engage national bodies, partners, stakeholders and Ministry of Health focal points (diagnostics and programme). Schedule and convene regular meetings. Develop communication pathways.
TWG establishment	<ul style="list-style-type: none"> Establish or identify relevant TWGs. Develop clear terms of reference with roles and responsibilities. Convene subject matter experts.
Challenges, goals and objectives	<ul style="list-style-type: none"> Define challenges and bottlenecks. Set goals and objectives (see examples below).
Policies and guidelines	<ul style="list-style-type: none"> Identify national policies and guidelines that are relevant to IVDs. Support and/or advocate for development of policies and guidelines. Seek government approval of policies and guidelines.
Governance	<ul style="list-style-type: none"> Discuss governance structure and mechanisms, including roles and responsibilities, accountability structures and harmonization. Promote adherence to standard procedures.

FIGURE 3 Process overview



5.1.1: Needs assessment

The existence of an agreed-upon National Multisectoral Strategic Framework, Health Sector HIV/AIDS Strategy, and National Care and Treatment Plan is crucial for ensuring that all partners involved in scaling up POC diagnostics have a shared understanding of the rationale for policy, strategic and operational priorities and decisions. In order to better understand the diagnostic landscape, one of the first steps is to conduct a needs assessment, which should include a close analysis of national and facility-level data.

Type of data to be gathered and analysed include the following:

- **National-level data**, such as disease prevalence, number of patients on treatment, national policies and practices, technology capacity, human resource capacity and whether POC testing is needed. If the answer to the 'if needed' is yes, additional information may include: consumption data of each type of assay and forecasted need for each type of assay (i.e., calculated using the number of working days in a year, and number of working hours in a day for devices, after-hours testing and human resources).
- **Facility-level data**, which may include patient numbers, current and potential demand for each type of assay at the facility level and distance from central testing laboratory. The minimum data for each site should be identified based on the current performance and requirements of the facility, including infrastructure, human resources, and supervisory and service requirements.

Other important issues to be addressed in the needs assessment include the extent to which existing policy guidelines and legal frameworks take POC technologies into account; political buy-in and stakeholder engagement for scaling up POC diagnostics; the local regulatory status of POC devices under consideration (e.g., local registration, quality assurance); operational requirements of introducing and scaling up POC technologies (e.g., the readiness and availability of potential sites, waste management capacity, device service and maintenance); and financial considerations (e.g., the availability of funds and sustainability).

5.1.2: Stakeholder engagement

The next step for introducing new POC technologies is to engage all relevant national bodies, partners and key stakeholders. This will ensure that stakeholders have an opportunity to provide inputs and participate in early decision-making processes, including policy and strategy development. In particular, it is important to identify the Ministry of Health focal points

who will lead the effort. In many cases, focal points should be identified in both the diagnostics or laboratory units and the relevant programmes, clinical or disease control units. It is also important to involve civil society, private entities, faith-based organizations, implementation partners and academic institutions, among others. Developing mechanisms (e.g., schedule regular meetings and communication; rotating chairs, etc.) to ensure active stakeholder participation will be critical for developing and sustaining momentum.

5.1.3: Technical working group establishment

Establishing or identifying a relevant TWG is strongly recommended. Based on respective national profiles and functions, the composition of the TWG should be diverse and ideally include (but not be limited to) representatives from the following areas:

- National ART, prevention of mother-to-child transmission and paediatric HIV care, treatment and diagnostic programmes
- Maternal, neonatal and child health programmes
- Central and reference laboratories
- Regulators
- M&E departments
- Implementing partners
- Supply chain logistics units
- Hospital and clinic staff
- Civil society
- Key funders

It is not necessary to have a separate POC TWG; if there is an existing laboratory TWG that is capable of assessing new diagnostics technologies, this group can be leveraged for POC technologies. If a separate POC TWG is established, however, it is important to develop clear terms of reference so that members understand their roles and responsibilities. Responsibilities may include reviewing product evaluation protocols and results; commenting and voting on policies and strategies related to POC systems and/or technologies; setting objectives; as well as developing implementation workplans/strategies, and clinical and diagnostic algorithms. One of the key responsibilities of the TWG will also be to convene subject matter experts (e.g., policies, national reference laboratories, diagnostic regulators, procurement and supply chain management, M&E, quality assurance, and human resources for health) to support the introduction, scale-up and integration of POC technologies into existing health systems.

5.1.4: Challenges, goals and objectives

Define the existing challenges, gaps and bottlenecks in the current diagnostics landscape, and then articulate the goals and objectives for POC technologies in a specific country in order to inform the strategic planning. This will be based on current HIV burden and challenges related to HIV testing for CD4, infant virological testing (including EID) and viral load. In general, the goal of introducing POC HIV diagnostics in a country is to accelerate critical clinical decisions by reducing the time from HIV diagnosis to ART initiation (for EID and CD4, where 'treat all' is not the policy), expediting adherence counselling, and/or identifying the need to change to second or third line treatment (for viral load). POC technologies also improve access to faster test results for all populations within the broader context of strengthening national laboratory systems and efforts to achieve the 90-90-90 Fast Track targets.

Examples of possible goals and objectives include the following:

Goals:

1. Decrease time from diagnosis/monitoring of ART;
2. Strengthened policies and coordination between programmes and laboratories (central and decentralized);
3. Decreased turnaround time for HIV diagnosis in infants;
4. Increased proportion of test results returned to patients;
5. Improved service delivery and supply chain logistics (i.e., reduced stock-out of test kits); and
6. Improved access and coverage of HIV diagnostic and monitoring testing.

Objectives:

1. Simplified patient care and treatment work flows;
2. Decreased loss to follow-up between infant HIV diagnosis and ART initiation;
3. Decreased AIDS-related morbidity and mortality (children and/or adults);
4. Increased retention in care; and
5. More appropriate switching to second line, less drug resistance, etc.

5.1.5: Policies and guidelines

National health/HIV policies and strategies define country HIV testing guidelines. Understanding if and how POC diagnostics are part of national policies is important to promote scale-up. Stand-alone POC policies and



guidelines may exist or they may form a component of broader strategies for HIV diagnostic and health services. The TWG should support policy and guideline development, in line with international standards and updated global guidelines. Diagnostic policies should be flexible to allow for the introduction of new POC technologies as they become available.

Stakeholders who are not responsible for developing or updating national policies can advocate for their development by highlighting the need for dedicated policies and strategies to guide Ministry of Health officials and implementing partners in incorporating POC technologies into diagnostic and clinical networks and to pertinent tools for policy development. Standardized guidelines and processes should be developed for the planning, implementation and evaluation phases for POC technology introduction, so that they are consistent across partners. Once developed, the policy documents will require approval by the Ministry of Health and dissemination to key stakeholders.

5.1.6: Governance

The TWG should meet regularly to discuss governance and the respective roles and responsibilities of members, with accountabilities for transparency and harmonized governance. Regular meetings and discussions promote adherence to standard procedures and allow members to share their experiences and concerns. To ensure better governance, building consensus with stakeholders from all levels is critical. Enabling all stakeholders to contribute to the governance process and to agree on the outcome will help overcome many barriers.

TABLE 8 Strategy and planning

DOMAIN	SUMMARY OF RECOMMENDED ACTIVITIES
Programme integration and laboratory coordination	<ul style="list-style-type: none"> • Leverage TWG to ensure coordination across national programmes and laboratories. • Convene regular meetings to review and develop joint operational plans.
Operational plan development	<ul style="list-style-type: none"> • Develop country operational plan with key stakeholders. • Ensure plans include key country information (existing policies, performance, targets, current coverage/capacity, and funding allocations), a timeline of activities (regulatory approval, pilots and scale-up plans) and other elements (partner roles, resource mobilization, costing and sustainability).
Diagnostics network mapping	<ul style="list-style-type: none"> • Conduct a granular mapping of laboratory network and diagnostic capacity to understand coverage levels, turnaround time for test results, throughput, and access to services. • Use information to understand gaps and strategic POC placements.
Product and site selection	<ul style="list-style-type: none"> • Identify primary objectives of integrating POC technologies, such as increasing patient coverage, access to testing, or cost efficiency. • Leverage tools and analysis to identify appropriate sites for POC placement and relevant products to achieve country goals. • Explore different POC placement models.
Budgeting and planning	<ul style="list-style-type: none"> • Draft a budget to include POC devices, associated commodity costs, service and maintenance, connectivity, wastage and buffer stocks. • Review budget regularly and ensure funding mechanisms are aligned to targets set by TWG.
Resource mobilization and advocacy	<ul style="list-style-type: none"> • Develop tailored communication packages to mobilize resources and engender a rapid and sustainable uptake of POC technologies. • Design advocacy efforts to target different stakeholders and demand creation at various levels.

5.2 STRATEGY AND PLANNING

Once the needs assessment has been completed, stakeholders have agreed on key priorities, and accountability structures have been defined, strategic planning begins based on national goals and objectives.

5.2.1: Programme integration and laboratory coordination

Conventional laboratory-based technologies provide testing to many patients and form the backbone for national testing services. As described in the previous section, it should be the role of the TWG to ensure that systems are in place to coordinate between and across national programmes and laboratories. The TWG's role should include convening regular meetings among required programmes and laboratories to plan, develop and review joint operational plans. National updates and challenges relevant for POC technologies should be discussed to ensure efficient, aligned and quality-assured programmes.

5.2.2: Operational plan development

It is essential to guide and structure project implementation, developing a detailed country operational plan, including mapping of key activities, such as regulatory approvals as well as pilot and scale-up planning. It will also help in understanding the baseline for proposed targets and to elaborate specific activities for achieving programme outcomes. The operational plan should include all relevant information and data on existing policies; current programme performance; clear activities and targets; assessment of laboratory capacity and testing efficiency; treatment coverage; and funding allocations and commitments – all plotted against timelines. It should also clearly define the role of partners, be costed, and include a resource mobilization plan.

5.2.3: Diagnostic network mapping

A comprehensive assessment of the national laboratory network and existing diagnostic capacity is key for strengthening national testing services. As a complement to the needs assessment – which will provide a broad view of the diagnostic landscape through an examination of patient- and facility-level data as well as the policy landscape – a mapping of the diagnostic network will provide a more granular understanding of existing diagnostic capacity, including mapping existing health facilities around the country with the current testing services offered. Understanding the performance of the different conventional laboratory-based technologies can help calculate efficiencies and current

throughputs for existing services. Moreover, although data availability may be limited, mapping coverage, turnaround times and access to these central/conventional laboratory services across facilities with programme performance will help set a baseline and strategically define the placement for POC technologies. Diagnostic network mapping can be undertaken in various ways, including: (i) visiting the facilities and mapping the variety of tests offered, referrals and equipment in use; (ii) distributing a survey to health facilities and laboratories to solicit this information; or (iii) using a geomapping software for highlighting distances between facilities and laboratories.

5.2.4: Product and site selection

When introducing HIV POC technologies, countries will need to determine which facilities will benefit the most from the introduction of POC testing and to determine the most appropriate type of POC device, based on the available products and suitability for identified facilities. While these two processes can be conducted separately and sequentially, it is often useful for countries implementing POC testing to employ a combined process whereby decisions on optimal products and sites inform each other and are adapted over time as new products become available and new sites are considered.

The process of selecting products and devices should be conducted in a rational and transparent way, with the objective of maximizing impact, minimizing costs, and meeting programme goals. It is recommended that a quantitative tool and objective rating system are used to ensure that the product and site selection process can be clearly documented and explained.

It is also recommended that the product and site selection process be iterative, reviewed annually, and adjusted or revised as new technologies or priorities emerge.

Product selection

The selection of POC products should be objective and transparent, deploying the most appropriate products to sites to maximize their impact on patient access to testing. The POC TWG should be actively engaged in and/or leading the product selection decision-making process.

A transparent and objective product selection process is critical for two reasons. First, comprehensive product information, which may not be routinely available, is needed to make informed decisions on which products to adopt. While suppliers typically provide Ministries of Health with extensive marketing materials, decision makers in the diagnostics sector do

not always have sufficient information to make informed product selection decisions. Second, public funding may expect that public procurement principles be observed in the procurement of commodities. Ministries of Health have an obligation to demonstrate that a rational and transparent process has been followed to select products for procurement. Guidance for procurement of HIV and HIV-related in vitro diagnostics and related laboratory items and equipment have been recently published by WHO.²¹

POC products should be rationally selected in response to the specific needs and capacity of selected sites, as well as to ensure instruments are fit for purpose. For example, testing volumes will vary across sites and impact both product and site selection. In addition, some sites will have the capacity to provide a consistent supply of electricity, while other sites might have an irregular or sporadic electricity supply. These factors and others should be considered when selecting the appropriate product for each type of site.

Site selection

Site selection should take into consideration the primary objectives for integrating POC technologies into national testing networks. As discussed in the previous section, primary objectives could include: increased access to treatment, decreased turnaround time for test results, increased proportion of test results returned to patients, or increased access to testing, etc., with the goal of leading to improved health outcomes. In addition, current and potential future demand for testing should be considered in order to allow for both an efficient and proficient use of the POC instruments within their minimal and maximal capacity ranges. Realizing the benefits of same-day test results requires locating devices near or where patients receive care and treatment, which should be the primary objective of the site selection process. Countries may wish to explore laboratory system models that include device sharing,²² increased POC and near POC technologies at centralized laboratories with strong and reliable transport systems, and 'hub and spoke' models.²³

Site selection should weigh the relative importance of three broad strategies for prioritizing sites for POC deployment, including:

1. Patient coverage – defined as prioritizing highest-volume sites to maximize the percentage of patients that have access to a same-day on-site testing.
2. Universal access to testing – defined as prioritizing the most remote sites in the country to ensure that all patients have access to a diagnostic test and receive the results.
3. Cost efficiency – defined as prioritizing the sites where each POC device has sufficient utilization to ensure cost efficiency.

To help assess suitable facilities, the TWG may consult with district health officers, facility supervisors, laboratory staff and community health workers so they understand why and how the new technologies will be used. TWGs may also choose to use tools, such as standardized checklists, to assess the readiness and quality of facilities, including electricity availability and reliability, presence of secure storage space for the POC device, and number of trained health workers on site.

5.2.5: Budget and planning

Careful drafting of budget and plans and revisiting them at regular intervals is crucial. The proposed budget should be based on careful analysis and the cost for introduction and implementation of POC technologies within a specified period. The budget should be comprehensive, including both instrument and associated commodities (accounting for commodity wastage and expiry) as well as system costs (e.g., service and maintenance; quality assurance; data management; training and mentorship; and waste management). It should also include both existing and anticipated funding (e.g., domestic and international; other stakeholder projects that could contribute) for POC introduction and scale-up within a specified time frame. To ensure sustainability, planning and funding mechanisms should always be aligned to realistic targets set forth by TWG.

5.2.6: Resource mobilization and advocacy

Two key concerns for maintaining successful and sustainable long-term support for POC technologies and strong laboratory systems in a given country are sufficient funding and effective advocacy and messaging.

Targeted communication and advocacy materials should be developed in order to mobilize resources and facilitate a rapid and sustainable uptake of POC services, and advocacy efforts should ideally target demand creation at different levels (e.g., national government and political leaders, the private sector, health providers, and communities served). It is recommended that an advocacy and communications workplan and calendar be developed, reviewed and updated annually.

5.3 REGULATORY APPROVAL

Regulatory oversight ensures that diagnostic technologies conform to established performance, quality and safety standards. Regulatory requirements are in place to prevent sub-standard technologies from being used for patient care.

The regulatory control of diagnostics generally has three components, including:

- *Pre-market assessment* to assess quality, safety, performance, benefits and risks prior to approval to market the device.
- *Marketing controls* to stipulate conditions under which devices can be offered for sale; to identify who may use the device and under what conditions; and to avoid inappropriate marketing or misleading claims regarding test effectiveness.
- *Post-marketing surveillance* to ensure the continued performance, safety and quality of approved products.

5.3.1: Global regulations

Several national, regional and global institutions develop quality, safety, efficacy and environmental protection norms and standards for IVDs that are recognized worldwide. These institutions may issue certificates that indicate conformity with such norms and standards. For example, WHO Prequalification indicates that an IVD meets global standards of quality, safety and efficacy. The Conformité Européene (CE) marking indicates

TABLE 9 Regulations

DOMAIN	SUMMARY OF RECOMMENDED ACTIVITIES
Global regulations	<ul style="list-style-type: none"> • Work with local regulatory authorities to consider adoption of existing global regulatory standards and leveraging their findings for POC technologies. • Consider participation in regional and/or global regulatory networks to streamline regulatory decision making.
National authorization for use	<ul style="list-style-type: none"> • Submit product dossier and relevant performance evaluation reports (if required) to the national regulatory agency (if present) or other appropriate national entities (e.g., Ministry of Health). • Register products with a national regulatory body (if present) or otherwise seek national approval for use.
Post-market surveillance	<ul style="list-style-type: none"> • Define appropriate proactive and reactive post-market surveillance²⁴ methods to anticipate potential issues and respond to product issues. • Design procedures for post-market data collection about device performance.



compliance with standards of the European Economic Area. Other institutions also play a regulatory role. For example, the United States Food and Drug Administration (FDA) sets and enforces standards for IVDs used in the United States. The certificates/approvals issued by these institutions can be used to guide the selection of POC technologies. By improving transparency of the regulatory review process while using harmonized norms and standards, the approval of POC IVDs across multiple countries may be accelerated with minimal duplication of efforts.

To register high-quality POC diagnostics, the national TWG can work with the local regulatory authorities to consider existing global regulatory reviews and approvals of POC technologies. If national regulatory capacity is limited, available guidance and outcomes of reviews by WHO Prequalification and/or other stringent regulatory agencies (FDA, European Union, Therapeutic Goods Administration of Australia, Ministry of Health, Labor and Welfare of Japan, Health Canada) can help to guide decisions on setting minimum standards for candidate technologies to meet. Participating in a regional and/or global regulatory network can also help local authorities streamline regulatory decision making and significantly reduce costs by eliminating the need for a duplicated review of product dossiers, quality system audits and performance evaluations, thereby reducing regulatory burden on IVD manufacturers.

5.3.2: National authorization for use

National registration of manufacturers and their devices is a basic regulatory requirement for any IVD. Manufacturers seeking national approval for a given IVD are generally required to supply a dossier to

the appropriate national regulatory authority describing the product and documenting evidence relating to the quality management system under which the product is manufactured, as well as the safety and performance (including stability) of the components.

However, it is not necessary for the performance of POC technologies to be evaluated in all countries seeking to introduce these new technologies into their national testing services. Rather, to simplify processes and where possible, it is recommended that national regulatory agencies leverage the results of dossier review and/or performance evaluations from other countries to grant regulatory approval in their own countries, thereby accelerating the process to approve and introduce new products.

Current regulatory oversight of IVDs in low- and middle-income countries, however, is highly variable, and the pathways for regulatory approval are not always clearly defined. While most low- and middle-income countries will have a legal framework and a national regulatory authority to regulate medicines, the regulation of medical devices, which includes IVDs, is less common. In countries without a formal regulation or registration mechanism, it may be the Ministry of Health itself which grants in-country approval for use. In countries that do have an established national regulatory mechanism for medical devices, approval for IVDs can be both costly and lengthy. The lack of clarity surrounding the regulatory pathways can create unnecessary burdens on manufacturers and deter the introduction of new IVDs in countries.

Harmonizing regulatory processes across countries, where mutual recognition or reliance allows products completing registration in one country to be registered in another with minimum duplication, could be very helpful to streamlining and expediting national approval and registration processes.²⁵

It is important to note that although national authorization of use for given POC devices is a precursor to product selection of POC devices for programmatic use, these are distinct processes and should not be confused.

5.3.3: Post-market surveillance

Post-market surveillance aims to ensure that diagnostics continue to meet the same quality, safety and performance requirements as when they were initially placed on the market. WHO has developed normative guidance on the importance and range of post-market surveillance activities which emphasizes the importance of both reactive post-market surveillance²⁶ and proactive post-market surveillance. Reactive post-market surveillance refers to activities undertaken after an issue has occurred related to the IVD (e.g., complaint reporting/monitoring; end-user quality control programmes;

external quality assessment schemes; etc.), whereas proactive post-market surveillance refers to activities to look for potential issues related to the IVD before they take place (e.g., pre- and/or post-distribution lot testing).

To implement post-market surveillance, responsible parties will need to:

- Identify stakeholders (national regulatory authorities, manufacturers, end-users);
- Assign roles and responsibilities;
- Define appropriate post-market surveillance activities; and
- Prepare documented procedures for post-market data collection.

A system for complaint handling should be implemented for any product that is supplied to the national testing programme. It is critical that end-users report adverse events and product issues as soon as they become aware of them to enable manufacturers to conduct a root cause investigation and, if necessary, to conduct field safety corrective actions.

Reportable incidents and adverse events include:

- False negative results;
- Poor specificity (false positive results) when compared with manufacturer’s specifications;
- Higher-than-expected rate of error codes or invalid results;
- Misquantification (if quantitative assay); and
- Obvious product defects such as damaged packaging or illegible labelling.

For additional information on post-market surveillance, including template reporting forms, see <www.who.int/diagnostics_laboratory/postmarket/en/>.

5.4 ASSURING QUALITY AND DATA MANAGEMENT

A strong quality assurance and data management system, which includes device connectivity, is essential for monitoring and improving test performance, while a safety and waste management plan is essential for maintaining good waste collection and disposal practices and preventing unwanted hazards.

5.4.1: Quality management systems

A strong quality management system is critical for ensuring the accuracy and precision of test results produced through POC technologies. A fully integrated quality management system will include multiple

TABLE 10 Assuring quality and data management

DOMAIN	SUMMARY OF RECOMMENDED ACTIVITIES
Quality management systems	<ul style="list-style-type: none"> • Leverage TWG to design and implement a strong comprehensive quality assurance system, led by the Ministry of Health. • Ensure internal quality controls, external quality assurance, data connectivity, training, mentorship and supervision are key components of the national POC quality assurance system.
Data management	<ul style="list-style-type: none"> • Institute efficient data management systems to monitor POC technologies, improve forecasting and enhance performance. • Strengthen electronic methods for capturing data and Laboratory Information Management System integration. • Incorporate data management systems into national M&E frameworks, plans and policies.
Connectivity	<ul style="list-style-type: none"> • Ensure interoperability and integration with existing national laboratory information management systems. • Review data for performance management, forecasting, maintenance needs, user errors and quality assurance.
Safety and waste management	<ul style="list-style-type: none"> • Assess existing safety and waste management capacity and practices, both at central laboratories and POC sites, to ensure that POC waste is collected, stored and disposed of following WHO waste management guidelines.²⁷ • Ensure all POC sites, including mobile/community outreach POC units, have new safety protocols in place that adhere to national standards.

quality assurance approaches to form a comprehensive strategy. These may include internal quality control, external quality assessment, equipment management/maintenance, organization, purchasing and inventory, information management (discussed in detail in section 5.4.2), documentation and record-keeping, process improvement, customer service, facilities and safety, and personnel. In particular, internal quality control is used to monitor performance of the assay and quality of the

results and to detect and correct problems as they occur. Although POC technologies generally have internal quality controls, it is important to ensure that the POC technologies chosen during the product selection process contain sufficient internal quality control mechanisms to minimize the risk of reporting incorrect test results.

A distinctive feature of quality management systems is that attention is paid not only to detection and correction of problems as they happen, but also prevention of problems. External quality assessment is a system for the objective comparison of a laboratory's testing to an external agency or facility (e.g., peer group of laboratories or a reference laboratory). External quality assessment programmes help identify problems before they happen and use corrective actions to prevent the problems from happening during the test procedure. Such programmes may include proficiency testing, re-checking/retesting, or on-site evaluation.²⁸

In order to systematically scale up comprehensive quality management systems, and to ensure its success, impact and sustainability, the TWG should define, plan and oversee implementation of efficient quality assurance measures. As in other areas of governance, strong leadership and advocacy are crucial; the Ministry of Health should engage leadership at the highest level for the quality assurance programme.

As part of a strong quality management system, it is recommended that countries implement robust and comprehensive mentorship and supervision programmes. In particular, it is recommended that a certified national trainer be placed or identified within the testing network to perform periodic and/or targeted site supervision and to ensure that prompt corrective actions are implemented to address identified issues and improve the quality of testing. Trainers will be responsible for performing external quality assessment, mentoring, assessment for certification, data collection and logistics. Mentorship should also address linkage to care, patient flow, device maintenance, and any other issues that can hamper testing.

For a more detailed discussion of the importance of quality assurance for POC testing, see the recent African Journal of Laboratory Medicine Special Issue on Quality Assurance.²⁹

5.4.2: Data management

Data management is an integral part of managing records for any testing programme, including POC testing. Effective data management systems are critical for monitoring and improving programme performance; improving national forecasting and quantification, procurement and supply chain management; monitoring the quality of devices and operator performance; and monitoring service, maintenance and device downtime.

Apart from capturing records for all indicators associated with POC IVDs, the key components of effective data management systems include:

- Defining clear use of the data (prevents collecting data for the sake of collection which can be expensive);
- Adequate physical storage space (anticipated volume);
- Data capturing tools (e.g., forms, registers, reporting templates (paper-based, electronic));
- Accessibility (e.g., who has access, what can be shared, how data are retrieved, how confidentiality is maintained); and
- Data storage and security (e.g., how long records need to be stored, how data are protected).

Without data, a POC testing programme cannot be accurately reviewed for utilization, performance and quality assurance. All testing sites should use a standardized logbook documenting dates, operator, assay used (lot numbers and expiry dates), test kit controls and quality control results, test results and the status reported to the client. Many countries have implemented standardized paper-based logbook systems, but there are implementation gaps in how paper-based data within log sheets are used for quality assurance both at the site level and at the central level. Thus, programmes should seek innovative ways to ensure that the data captured for POC testing can be analysed and used for early detection of challenges. Options include connectivity, electronic methods of logging testing data at sites such as electronic logbooks linked to a laboratory information management system, and phone-based and non-phone based test readers that can capture results and send them to a central site for analysis.

As with other changes in national programmes, any new data management system should be incorporated and integrated into national policies and guidelines, including national M&E frameworks and plans. For additional information, see section 5.7 on Monitoring, Evaluating and Improving Quality.

5.4.3: Connectivity

Several current POC devices have the advantage of wireless connectivity, which contributes to and is a component of data management. Connectivity refers to the ability to transmit data from testing conducted at a given POC site to a central database. To minimize duplication and the creation of parallel data systems (which are often unsustainable), it is essential to ensure interoperability and data integration with existing national health information management systems.

Importantly, connectivity also allows for centralized management of the POC testing programme, as well as real-time M&E of decentralized POC testing. The data transmitted can be reviewed for post-market surveillance, device performance, logistical purposes (including supply chain management), service and maintenance needs, quality assurance, etc. Depending on the device, it can be used for tracking deviations in internal quality controls; forecasting; post-market surveillance; inventory management; determining error rates and types both by operator and site; determining usage and equipment downtime; alerting to the need for device repair; and determining user profiles and the effectiveness of training and certification. Importantly, the usefulness and impact of connectivity of POC testing depends on reliable information and communication technology infrastructure. This includes telecommunications network coverage, a robust central server and data security protocols. The effective use of real-time data for proactive monitoring, as well as for the identification and implementation of corrective actions and targeted supervision, requires regular data review and utilization by programme managers. Regular meetings at predetermined intervals and/or electronic alerts that are directly sent to programme managers are some of the ways that can be used to encourage managers to review POC data regularly.

5.4.4: Safety and waste management

The development of a safety and waste management plan is essential for preventing unwanted hazards and maintaining good practices. It is likely that several POC sites will already have safety and waste management standard operating procedures (SOPs) in place, with established processes and collection points for given specimens and medical waste. In some cases, existing protocols only need to be reiterated or modified upon deployment of POC technologies. In other cases, sites and other service delivery mechanisms, such as mobile units or community outreach with POC devices, will require new SOPs to ensure adherence to standards.

Importantly, the waste management requirements of different POC nucleic acid testing systems require careful consideration when making decisions about product selection. Some nucleic acid amplification assays use guanidinium thiocyanate to facilitate extraction of DNA and ribonucleic acid from cells. Found in test cartridges and/or external reagents, guanidinium thiocyanate is a harmful chemical which must be disposed of through high temperature (at least 1,000 °C) incineration. Without proper disposal, the chemical can be hazardous to individuals and the environment, including the water supply.



TABLE 11 Procurement and supply chain management

DOMAIN	SUMMARY OF RECOMMENDED ACTIVITIES
<p>Procurement methods</p>	<ul style="list-style-type: none"> • Develop a procurement strategy and identify appropriate procurement methods. • Solicit offers in a transparent manner and establish vendor capacity. • Leverage existing tools and templates to standardize bid receipt and evaluation processes. • Select vendor and conduct contract negotiation and signing. • Establish delivery schedules, shipping and cost details.
<p>Forecasting and supply planning</p>	<ul style="list-style-type: none"> • Coordinate and understand supply chain investments and key players to maximize economies of scale. • Collaborate with procurement officers, non-governmental organizations, national budgets and other donors to identify the best method for purchasing, such as pooled procurement or pre-negotiated pricing through consortiums. • Develop a national POC supply plan with quantities, costs, delivery times and arrival dates. • Factor production capacity, lead time, seasonal changes, customs delays, buffer stock and logistics information into the supply plan. • Revise budgets regularly to match the supply plan.
<p>Warehousing and inventory management</p>	<ul style="list-style-type: none"> • Ensure POC IVDs are introduced in a sustainable manner without compromising existing national supply chain systems. • Follow national procurement and supply chain guidelines for management and storage of POC IVDs. • Integrate POC IVDs into sample transportation networks and referral systems that exist for remote health facilities or create new approaches for POC IVD delivery. • Train health workers at new POC sites to appropriately manage and track POC devices and associated commodities.

5.5 PROCUREMENT AND SUPPLY CHAIN MANAGEMENT

A key component of introducing new POC technologies into national and laboratory systems is procurement of the devices and commodities, forecasting and supply planning, as well as warehousing and inventory management. Key recommended activities pertaining to each are noted below.

5.5.1: Procurement methods

Once products have been selected, the next step is to develop a procurement strategy. It is important to:

1. Choose suppliers based on their ability to provide specific equipment, reagent, and consumables required to perform the assay and to provide after-sales support.
2. Apply procurement methods and sourcing strategies to ensure a fair, transparent and competitive process as well as best value for money. For the regular supply of reagents and other consumables for the selected equipment, consider the use of framework contracts (bundling of services/duration/commodities/consumables, etc.) to reduce procurement efforts and build strong supplier relationships.
3. Consider the total cost of ownership in addition to the purchase price when taking purchase decisions. If available, reagent rental or equipment leasing models reduce the upfront capital investment and can ensure ongoing quality and responsive service and maintenance, as well as future upgrades of the equipment.
4. Award contracts and place orders to ensure that products are available as needed.

Although separation of requisitioning and procuring entities is essential to safeguard a transparent procurement process, there is need for collaboration between the two to define product specifications. It is good procurement practice to develop generic specifications so that the procurement process allows full and open competition for all products (i.e., multiple vendors) meeting minimum specifications.

There are several procurement methods, and the most appropriate one must be selected in each case and for each product according to several criteria. The procurement method will vary depending on the product. The selection of the procurement method and subsequent drafting of the solicitation document should consider:

- **The category of the product:** Is the product multi-source or single-source? This determination is based on whether or not there is competition in the market for the product.

- **The value of the procurement:** In general, beyond a certain threshold, it is not possible to award a contract directly, and competitive bidding through invitation to bid is required by law.
- **National requirements**

Table 12 below details the various procurement methods that can be used, depending on the considerations noted above.

TABLE 12 Different bidding methods for products

BIDDING METHODS	DESCRIPTION
Request for quotation	Used for low-value procurement of simple products and services with standard specifications.
Invitation to bid	Used for acquisition of products and services with standard specifications.
Request for proposal	Used for acquisition of products or services for which the requirement cannot be clearly defined.

In the case of some POC technologies, competition may be restricted to a limited number of vendors or a specific product from one vendor. Due to the current limited options for POC, it may be necessary to solicit a single source (single vendor) for POC technologies. It is critical, for the purposes of integrity and transparency, to issue a *Notification of Intent* limited-source procurement so that vendors may have an equal opportunity to review the requirements to determine if they can provide substitute products (this requirement should be met even if there is only a single product that clearly meets the requirements).

Several methods can be used to solicit for offers. Due to the limited number of supplies for POC technologies, the most appropriate method is the Request for Quotation.

The United Nations Procurement Manual,³⁰ the harmonizing United Nations procurement guidelines³¹ and the WHO guidance for procurement of in vitro diagnostics and related laboratory items and equipment,³² for example, provide tools and templates which can be used for the development of bid

documents (Note: where available national guidelines should be followed; UN tools may be adopted or adapted where a national policy does not exist).

All implementing partners using Global Fund grants to procure are required to follow their procurement and supply chain management policies. For more information, please visit the Global Fund’s website: <www.theglobalfund.org/en/>.

In terms of pre-selecting vendors, it is recommended that potential vendors be identified fairly and transparently. Bid evaluations should be conducted to establish vendor capacity, compliance with manufacturing standards, experience and past performance. Vendor evaluations are particularly important in POC testing, as the nature and placement of the devices differ greatly from conventional technologies. For example, a vendor with significant experience supplying equipment and consumables to the referral level (Figure 2, level 3 or 4 of the laboratory network) may not have the capacity to service and maintain numerous POC devices at the periphery (Figure 2, level 1 or 2 of the laboratory network). In addition, bid receipt and evaluation processes should be standardized for POC technologies and follow national guidelines; any changes should be documented and relevant parties notified. For full competition (i.e., where multiple products exist), evaluations should be conducted in two stages, and ideally by different entities.

A technical evaluation (Stage 1) is needed to ensure that the diagnostic product meets minimum requirements as defined by the technical specifications and focuses on the performance and operational characteristics,³³ while a **vendor evaluation (Stage 2)** is needed to ensure supplier capacity to perform appropriate installation and training, and provide service and maintenance and a reliable supply. Only technical proposals that pass the technical evaluation stage enter the vendor (or supplier) evaluation phase. The evaluation also needs to evaluate pricing, with consideration given to shipping, installation, training, servicing and maintenance. If two or more vendors are closely competitive in the evaluation, consider a split award. This will keep competitors in the market for future opportunities, and reduce dependency on a single supplier, thereby reducing supply side risk.

The final steps in the procurement processes include notifying bidders of the award, entering contract negotiations and signing. Contract negotiations may include determining the delivery schedules, required INCOTERMS, and shipping mechanisms to reduce cost. Other cost-avoidance opportunities may be negotiated to ensure limited exposure to market price variability due to factors such as inflation and currency fluctuations.

Procurement contracts should also consider clauses for replacement of defective products (either through field safety corrective actions or otherwise) and disposal of obsolete products and instruments.

Furthermore, procurement contracts for instrument-based IVDs should include clauses for the following aspects:

- Installation and calibration;
- Provision for pre-service and in-service training;
- Preventive and corrective maintenance; and
- Warranty terms.

5.5.2: Forecasting and supply planning

Forecasting involves planning demand based on programmatic needs, allocated funds, consumption and estimated growth. As described earlier in the Data Management section, it is important to have reliable and accurate data reflecting the number of patients on treatment, and new patient targets to calculate the volume of tests, including a buffer stock, needed to meet the programming needs. It is also crucial to discuss the supplier's total production volumes across countries to ensure adequate manufacturing capacity and on-time deliveries.

The supply plan includes specific details on the quantities of equipment and supplies required, supply chain costs, delivery lead times, and expected arrival dates of shipments to ensure procurement and delivery schedules that do not result in service breaks. Coordination of supply chain investments is a critical first step in developing the supply plan. Input from national and regional stakeholders can help maximize economies of scale, particularly where global, regional and national policies dictate negotiated pricing. It is important to consider the following:

- Collaboration with planning and procurement officers to negotiate the best possible price for forecasted need;
- Optimizing pricing through pooled procurement on a regional or global scale;
- Pre-negotiated pricing through EID and viral load POC procurement consortium, non-governmental organizations such as the Clinton Health Access Initiative (CHAI) and the Foundation for Innovative New Diagnostics (FIND), and the Global Fund's Pooled Procurement Mechanism (other organizations and/or systems may exist in the future to access pre-negotiated pricing information);
- National budget available for POC testing; and

- Financial inputs from donors.

POC technologies deserve special attention concerning price negotiations when the volume of devices, equipment and consumables may be significant to cover multiple sites across a country.

Budget preparation and supply planning are activities that are interdependent. If the budget does not cover the forecasted demand, it will be necessary to revise quantities or find a mechanism for increasing the available budget or reducing costs.

In developing a supply plan, key considerations include:

- Possibility of extended lead times for novel products – i.e., production capacity may be limited especially if the POC manufacturer is new to the market;
- Consideration of lead time down to the end-user level, which may be considerable where products must reach small, remote areas;
- Impact of seasonal changes (e.g., rainy season) on delivery, especially to remote sites;
- Communication time and mechanisms for reorder (i.e., the time logistics information takes to reach personnel responsible for initiating an order);
- Mechanism for collecting and communicating logistics information from remote locations;
- Possibility of delays once the devices/reagents have arrived in-country, due to customs and government approval processes; and
- The need to adjust conventional instrument forecasts to account for shifts to POC instruments where sites previously referred samples.

5.5.3: Warehousing and inventory management

In terms of warehousing and inventory management, it is important to manage the introduction of POC products in a way that does not compromise existing supply chain management systems or introduce parallel systems that are unsustainable. POC products are no different from regular items in that they must be properly accessioned and stored in a warehouse. Good storage practices for POC products should follow national procurement and supply chain management guidelines (where available) for the appropriate management, storage, stock rotation and security of POC products. It is also important to adhere to manufacturers' recommendations on storage conditions, such as temperature, humidity and exposure to sunlight. Understanding reagent shelf-life is essential to

design frequent delivery schedules that recognize this possible constraint and avoid wastage.

The delivery of diagnostic products to remote and widely disbursed sites presents a major challenge for supply chain systems. POC technologies and supplies may require new approaches to delivery or integrating with existing sample referral networks, such as motorbikes and volunteers. The product selection exercise can consider existing distribution mechanisms already in place, such as vaccine delivery, HIV diagnostic and treatment delivery, or other health facility commodity delivery systems.

The so-called ‘last mile’ of distribution (the final leg of distribution) could be the most significant and the costliest for POC products, as with other health facility commodities. Utilizing existing delivery capacity is important. However, the potential added burden on district-level staff (if applicable) – including accessioning, unpacking, repacking and issuing products to multiple centres – must be considered.

Appropriate and sufficient space will need to be identified at the POC to store sufficient cartridges at the appropriate temperature, taking into consideration the volume of different manufacturers’ cartridges.

POC technologies need careful planning for inventory management of devices, cartridges and other accessories. A centrally connected commodity management system is preferred for accurate response. A number of basic inventory tools (manual or computerized) can be used to manage inventory.

Lastly, programme and facility managers should carefully track usage of POC products to limit waste, and prevent both stock-outs and expiries. Facility staff administering POC testing should be trained on consistently using ‘first-expiry-first-out’ stock practices. Programme planners should focus on developing a logistics system for POC that works within the existing system, so as not to further complicate processes. Existing requisition and reporting forms may require adaptation for POC products.

5.6 IMPLEMENTATION

To prepare for implementation, countries should plan activities to ensure that the POC technologies are introduced and scaled up in a strategic phased manner. Careful consideration should be given to service and maintenance agreements; human resource needs for POC testing; the development of clinical tools and SOPs; training, supervision, and mentorship plans and modalities; and a phased approach to scale-up.

5.6.1: Service and maintenance

It is critical to negotiate a contract for service and maintenance with the supplier during the procurement process. The terms of such agreements should be forward-looking and foster sustainability and functionality. These terms can include (among others) maximum downtime percentages; standards for the availability of trained personnel in-country

TABLE 13 Implementation

DOMAIN	SUMMARY OF RECOMMENDED ACTIVITIES
Service and maintenance	<ul style="list-style-type: none"> • Negotiate contract for service and maintenance during the procurement process that includes metrics for maximum downtime, repair times, and upgrading or replacing devices. • Ensure distributors and service engineers are in place. • Consider a single service and leasing agreement through Ministry of Health contract. • Weigh the merits and challenges of a swap-out model.
Human Resources	<ul style="list-style-type: none"> • Work with the Ministry of Health and TWG to identify human resource needs. • Identify and propose methods to ensure enough human resources for POC testing needs.
SOPs, training and mentorship	<ul style="list-style-type: none"> • Use TWG to plan POC deployment and integration into national testing algorithms and policies. • Design SOPs for confirmatory testing and inventory management. • Develop a training landscape analysis, detailed training plan and training package. • Ensure comprehensive training tools, mentorship and supportive supervision are made available to each POC site to address end-user needs, clinical workflow and facility-specific issues.
Phased scale-up	<ul style="list-style-type: none"> • Design a phased approach to scale-up to maximize learning, identify actions for course correction and promote sustainability. • Document lessons learned and best practices to inform future scale-up efforts.

to repair devices when necessary; agreements to swap out broken devices temporarily so downtime is limited while repairs are made; agreed-upon standards for repair time; frequency of spot checks for quality control; and agreements for replacing or upgrading devices after a set amount of time. It is beneficial that manufacturer-approved in-country distributors and service engineers are in place before procurement and uptake occurs. Suppliers should also identify local agents responsible for checking on the equipment periodically, and operators at each facility should learn the basics of maintenance and equipment handling during their trainings. In addition, cartridge and service bundling arrangements and network/system negotiated rates should be explored over conventional per instrument service and maintenance approach for POC devices.

A single service and leasing agreement for the public sector can help reduce administrative and operational issues. This will, however, require that all procuring stakeholders adhere to the same terms and conditions, ideally through a formal contract between the Ministry of Health and a single service provider.

The goal of a repair model is to keep site downtime as low as possible. One example of a repair model is a swap-out model, whereby a backup pool which can quickly swap faulty devices is kept at regional hubs while faulty devices are removed for repair, usually to a centralized service centre. In some cases, the backup pool could be negotiated through the supplier as part of the service maintenance plan. Technical hotlines can serve to assist in repairs that can be done on-site. Other considerations include the cost benefit of moving a device (perhaps via courier service committed through the service and maintenance agreement) vs. sending a technician to the POC site.

5.6.2: Human resources

The TWG must closely work with the Ministry of Health and other national health workforces (e.g., clinicians, laboratory technicians, community health-care workers, etc.) for the identification and coordination of human resource needs. Countries have various arrangements for what constitutes health workforce for laboratory/diagnostic services. This might include lab technicians, clinicians and, in some instances, from physicians to nurses or lay people or community health workers through task-shifting policies. The TWG along with relevant officials should propose SOPs and resource existing health-care staff to meet its POC testing needs. Human resources for health include individuals working in the private and public sectors, those working full time or part time, those working at one job or holding jobs at two or more locations, as well as those who are paid or provide services on a volunteer basis.



5.6.3: Standard operating procedures, training and mentorship

The TWG will need to decide how POC technologies should be integrated into the national testing algorithm, and specifically how the required confirmatory testing of positive infant virological test results will be done. Through the quality assurance activities, if performance of the POC devices are determined to be good, the POC could be streamlined similarly to other laboratory technologies. In addition, SOPs for testing and inventory management should be updated or developed, as well as job aids to support clinical workers in implementing POC testing. Only trained operators should use the technologies, and informal training of colleagues should be discouraged. Finally, POC testing should be incorporated into supervisory checklists to support the performance monitoring and improvement of POC instruments and clinic staff.

In terms of training, it will be important to develop: (1) a training landscape analysis (*see below for details*); (2) a detailed training plan; and (3) a training package. Hands-on training is important for all operators.

A training landscape analysis helps identify country capacity, needs and resources, especially regarding remote settings. The training landscape analysis could include information about the following areas:

- Number and location of key health workers and trainers;
- Number and location of the supervisors of key health workers;
- Existing training capacity and trainers at different levels of the health system and facilities;
- Location and capacity of training centres, colleges and vocational schools;

- Possible role for implementing partners and institutions of higher education in developing curricula and providing master trainers; and
- Decentralized training systems for quality assurance, use of connectivity technologies such as modems, and SMS in POC training.

Successfully introducing POC testing in a facility requires more than technical training on the use of the new technology. Training for POC testing goes beyond simple operation of a device. It also addresses key changes that need to be made where facilities shift from conducting testing through sample referral to conducting testing on-site or augment their central laboratory capacity to include POC devices. The four elements of training for POC testing are:

- **Technical training** which teaches POC operators how to operate the technology itself.
- **Lab systems training** which teaches POC operators and support staff how to integrate and adapt existing laboratory systems with new POC systems to experience ongoing success, including laboratory data systems.
- **Clinic systems training** which brings together all human resources involved in HIV services to discuss the changes to patient flow and clinic management that should be made for the introduction of POC testing to have the greatest patient impact. This is an area of particular importance as introduction of a new activity can impact the wait times and flow of patient care.
- **Certification** of operators having successfully completed training and demonstrated capacity is strongly recommended. In addition, recertification or refresher training models should be considered every 12 or 18 months to ensure quality, to address staff turnover, which may occur, and to minimize informal on-site ‘training’ of uncertified operators.

An effective POC training programme should consist of three different phases and emphasize clinical training, hands on training and mentorship/supervision:

- **Training of Trainers:** The roll-out of training for introducing a new POC technology most often begins with one or more Training of Trainers, in which a group of local trainers is trained by ‘Super Trainers’ from the manufacturer, the suppliers, the Ministry of Health or implementing partners. Generally, trainers will be brought together from every region of the country so that they can then be deployed to train in their respective regions. After trainings are completed, regional trainers can continue to be involved in mentorship programmes in

their region.

- **End-user training:** Effective end-user training not only improves the patient impact of introducing POC technologies, but it can also save money in a national programme. Training can reduce error rates and improve documentation and patient receipt of results, reducing wastage of cartridges for repeated tests and human resource time spent on results that are never received. There are various models for end-user training, including on-site training; off-site training; hybrid on-site and off-site training; and a combined regional off-site Training of Trainers and training model.
- **Mentorship:** Regardless of which training model is used, after initial training has been completed, the trainers should revisit each facility periodically to provide mentorship. During the mentorship, trainers assess key challenges that the facility is facing and focus efforts on addressing those challenges with the health workers. Some facilities may have high error rates or poor sample collection technique and require follow-up technical mentorship. Other facilities may need help with data management because they have weak filing systems or bad communication between the facility and ART clinic. Mentorship covers many of the same technical, laboratory and clinic systems topics covered in the training, but should be targeted specifically to each facility’s needs.

Once the training model is designed, a detailed training plan should be developed. The training plan should identify required resources, estimated timeline, and the individuals at each site who will be responsible for operating POC devices. This should be done carefully, to avoid overloading existing activities and responsibilities of existing staff. If necessary, a new cadre may be created to operate the devices. The entire process from Training of Trainers to operator certification to deployment to mentoring may be assisted by having regional focal persons.

At the time of this writing, most of the currently available POC technologies require device specific-training curriculum for their use. As these technologies become more widely available and in-use, training and re-training curricula will require less device specificity. Performance measures that identify end-users with the capacity to perform the test accurately and precisely should also be developed.

5.6.4: Phased scale-up

When introducing a new intervention or technology into an existing health or laboratory system, a phased approach to scale-up is recommended. A phased approach allows for the progressive integration of the new

technology and associated programmatic interventions into the existing health system, allowing for monitoring and course corrections should problems be identified. An implementation pilot should be the first step in a phased approach. Through an implementation pilot, countries can identify common challenges and bottlenecks to POC integration; identify corrective actions needed; and establish best practices. Lessons learned during the piloting phase as well as through operational/implementation research can then be used to guide and inform broader scale-up efforts. However, given the urgent need, it is recommended that lessons learned from other programmes be used, where possible, to set aggressive timelines for the introduction of POC products.

5.7 MONITORING, EVALUATING AND IMPROVING QUALITY

Monitoring and evaluation (M&E) of POC testing will ensure quality and effectiveness of national testing programmes. A robust M&E system is required from the onset of the programme to support the collection of appropriate and high-quality data for evidence-based decision making, optimal allocation of resources, programme expansion and, ultimately, the continuous improvement of processes. Beyond the implementation and scale-up of the programme, M&E can serve as a catalyst for wider health system strengthening by building country capacity to generate and use data to test, implement and expand health improvement programmes in the future.

Monitoring is the routine and systematic collection and analysis of predetermined processes, and output and outcome indicator data to assess progress made towards programmatic targets and goals. Data generated through routine monitoring provides stakeholders with an overview of trends and patterns in order to support evidence-based decision making for programme management and promote internal and external accountability and learning. Routine monitoring data are an essential starting point for the programme's evaluation.

Evaluation is an objective assessment of a project or programme's design, implementation and results. An evaluation helps determine a project or programme's relevance, effectiveness, efficiency and/or impact. For example, it would be useful to evaluate the impact of POC testing on the national EID programme, including the effect of POC testing on timeliness and rates of ART initiation for HIV-positive infants. Countries could also decide to evaluate individual approaches for implementing POC EID testing, such as the feasibility of EID testing on polyvalent platforms and whether offering POC EID testing outside of traditional prevention of mother-to-child transmission services facilitates increases identification of HIV-exposed and HIV-positive infants.

TABLE 14 Monitoring, evaluating and improving quality

DOMAIN	SUMMARY OF RECOMMENDED ACTIVITIES
Develop an M&E framework and operational plan	<ul style="list-style-type: none"> • Develop an M&E framework with appropriate indicators linked to programme activities, outputs, outcomes and goals. • Create an M&E operational plan through a consensus-building process with all relevant stakeholders. • Include how progress will be measured, data collection activities, timeline, costs, reporting requirements, and human resource needs. • Implement the M&E plan at the start of the programme.
Collect and analyse data	<ul style="list-style-type: none"> • Carry out baseline data collection for benchmarking. • Implement efficient and robust data collection and avoid duplication. • Develop mechanisms to ensure data quality. • Consider planning for additional data collection activities, as needed.
Disseminate data, devise improvement plan, and update M&E plan	<ul style="list-style-type: none"> • Leverage TWG to review and discuss data and progress regularly. • Disseminate data for transparency and to inform progress towards goals. • Update M&E framework as necessary to ensure alignment with the programme's strategic goals.
Implement changes and improve quality	<ul style="list-style-type: none"> • Use data collection and evaluation findings to improve programme activities and implementation, and make adjustments.

Baseline and routine data analysis and reporting may use clinic registers and patient cards. Ideally, where possible, monitoring using electronic systems should be implemented. As noted in the earlier Data Management section, routine collection, analysis and review of data is critical to ensure efficient and effective delivery of services, for POC and all health-related services. Stakeholders must also adhere to country-specific requirements about accessing and reporting indicators based on patient-level data, which in some contexts may require ethical approvals. The use of unique patient

identifiers (numbers) is one approach that can be used to identify and track patients as they move through different facilities while also protecting the privacy and confidentiality of patient information.

If research studies are planned or undertaken as part of M&E, all ethical approvals must be secured and research protocols approved by authorizing entities (e.g., Ministry of Health; academic or research institutions, etc.) prior to the initiation of the research.

5.7.1: Develop a monitoring and evaluation framework plan

A monitoring and evaluation plan should be developed and implemented as soon as possible, preferably at the start of the programme. The M&E plan should be developed through a consensus-building process with all relevant stakeholders (even if not part of the M&E team or POC TWG) to avoid partners' reporting data that are incongruent with the national POC programme or strategy. A useful starting point is the development of an M&E framework which contains indicators and targets that are linked to the programme's activities, outputs, outcomes and overarching goals; suggested programme indicators are delineated in Table 15 below. It is recommended that indicators include disaggregated patient-level indicators, aggregated patient-level indicators, product/platform process indicators, market indicators, and country and global programme-level indicators. This framework, coupled with a project logic model,³⁵ allow the M&E team to determine activity timelines, assess required data collection procedures, and define appropriate data sources and reporting frequencies over the course of the programme. Information generated through the framework and logic model can help inform the M&E operational plan.

The M&E operational plan should describe:

- How the programme will measure progress towards, and achievement of, its goals and objectives, as stated in the programme's strategic plan;
- Data collection, management, analysis, use and quality assurance activities with related timelines;
- Key evaluation questions and approaches to help ensure strategic evaluation implementation;
- Available human resources and M&E-related roles and responsibilities;
- Estimated costs of M&E activities to ensure that they receive sufficient resources within the programme; and
- Reporting requirements, timelines and content.

5.7.2: Collect and analyse data

An efficient and robust data collection, management and analysis system should be implemented, keeping in mind the tools and systems already in place in-country. Duplication should be avoided and collaboration with government agencies should be promoted. M&E efforts should be integrated with routine national data collection as much as possible. Once programme indicators have been selected, a data flow analysis which assesses the movement and collection of data within and across country programmes, starting from the original source – such as facility-level registers or purchase orders – may be helpful. This data flow analysis can inform the development of new or updated data collection tools and support the development of a data-quality check system at critical points across the data collection process. An indicator mapping exercise might also be useful if programme indicators do not match indicators routinely collected and reported in-country; this is especially useful if the programme is being implemented across multiple countries. Programme indicators should be collected, analysed and reviewed at regular intervals. In particular, the data collection and analysis plan should take into account the programme's phased approach, ensuring that data quality is maintained as the programme expands.

5.7.3: Disseminate data, devise improvement plan and update M&E plan

Programme data, both monitoring data and evaluation findings, should be disseminated and reviewed regularly by the management and stakeholders to close the feedback loop, assess progress and develop a continuous programme performance improvement plan, prescribing adjustments and corrections for quality improvement. Additionally, findings should be used to assess how the programme implementation speaks to the broader goals of addressing the 90-90-90 Fast Track targets.

Long- and short-term M&E and programme implementation plans should be updated periodically based on information resulting from M&E activities. The ability to improve the programme will depend on the availability of the right data at the right time, hence the importance of establishing an M&E framework that speaks to the programme's strategic plan and goals from the onset.

5.7.4: Implement changes and improve quality

Data collection and evaluation findings should be used for making improvements in programme activities and implementation at all affected levels. Any adjustments should be monitored and evaluated to determine if scale-up is appropriate.



TABLE 15 Example product, programme and impact indicators for POC technologies

PRODUCT INDICATORS	PROGRAMME INDICATORS	IMPACT INDICATORS
<p>Product and supplier performance based on contractual obligations, including:</p> <ul style="list-style-type: none"> • Percentage of time instrument was broken • Percentage of out-of-specification test performances during pre- and post-delivery testing³⁶ • Number of on-time deliveries; order lead time, etc. 	<p>Programme scale-up, including:</p> <ul style="list-style-type: none"> • Number of sites with connectivity • Number of sites successfully passing external quality assessment • Number of sites with routine supportive supervision or mentoring visits that address POC testing • Number of sites with error rates >5% • Number of POC devices in use • Number of total POC tests performed • Number of sites trained to perform testing • Number of POC devices connected • Number of health-care workers trained and certified to perform POC testing • Number of trained health-care workers performing POC testing • Number of POC tests performed on HIV-positive patients • Percentage of total HIV-positive patients tested for CD4 and viral load using POC 	<p>Programme impact, including:</p> <ul style="list-style-type: none"> • Number of patients initiated on ART • Number of patients receiving a POC test • Percent of patients receiving viral load, infant virological or CD4 tests (including newly diagnosed patients) and returning for follow-up • Average turnaround time between sample collections to results received by patients

Note: In some cases, monitoring and evaluation plans will require country ethics review approvals – see earlier example of patient identifiers that can be used.

ANNEX A: GLOBAL REGULATORY AND STANDARDS ORGANIZATIONS FOR MEDICAL DEVICES³⁷

- International Standards Organization (ISO): an independent non-governmental organization that promotes worldwide proprietary, industrial and commercial standards to safeguard consumers and end-users of products and services. ISO 13485 in particular sets the requirements and standards for the quality management system that an organization needs to demonstrate its ability to provide medical devices and related services that consistently meet customer and applicable regulatory requirements.
- The U.S. Food and Drug Administration (FDA) has two pathways for the introduction of medical devices on the U.S. market:
 1. Approval of class III devices through pre-market application: a 'valid scientific evidence' (21 CFR 814.20(b) (3) (vi)) presented by the manufacturer to demonstrate safety and effectiveness of the device.
 2. Clearance of class II and some class I medical devices through pre-market notification (510(k)): a less rigorous process that establishes substantial equivalence in intended use and technological characteristics of a new device to a legally marketed predicate device.
- Conformité Européenne (CE) marking: a declaration by a manufacturer that a medical device meets essential requirements set in corresponding Directives of the European Parliament (e.g., Directive 98/79/EC on in vitro diagnostic medical devices). Note that CE marking is prepared by a manufacturer and not by European Competent Authorities (Ministries of Health) or by the European Commission Directorate General Health and Food Safety; however, mechanisms exist to ensure validity of CE marking.
- WHO Prequalification (PQ) status means that an IVD satisfies WHO requirements for quality, safety and performance based on WHO review of product dossier, performance evaluation of the product, and inspection of a manufacturing facility. WHO PQ status does not imply approval to market or an endorsement of an IVD.

ENDNOTES

- 1 Joint United Nations Programme on HIV/AIDS, UNAIDS Fact Sheet July 2017, UNAIDS, Geneva, 2017.
- 2 Joint United Nations Programme on HIV/AIDS, *Prevention GAP Report*, UNAIDS, Geneva, 2016.
- 3 Phillips, Andrew, et al. 'Sustainable HIV Treatment in Africa through Viral Load-Informed Differentiated Care', *Nature*, December 2015, pp. S68–S76.
- 4 Infant diagnosis of HIV, which occurs four to six weeks after birth, is commonly known as 'early infant diagnosis' or EID, while 'infant virological testing' is used more broadly in this document to refer to nucleic acid testing, which occurs during the span of infancy (first year of life). Serological testing may be used for HIV diagnosis when the child is older than 18 months.
- 5 Based on weighted average of four countries, 43 per cent of EID test results are not received by patients. Mozambique: Deo, Sarang, and Milind Sohoni, 'Optimal Decentralization of Early Infant Diagnosis of HIV in Resource-Limited Settings' *Manufacturing & Service Operations Management*, vol. 17, no. 2, May 2015, pp. 191–207; Malawi: Dube, Queen, et al., 'Implementing Early Infant Diagnosis of HIV Infection at the Primary Care Level: Experiences and challenges in Malawi', *Bulletin of the World Health Organization*, vol. 90, no. 9, September 2012, pp. 699–704; United Republic of Tanzania: Nuwagaba-Biribonwoha, Harriet, et al., 'Introducing a Multi-Site Program for Early Diagnosis of HIV Infection among HIV-Exposed Infants in Tanzania', *BMC Pediatrics*, vol. 10, no. 44, June 2010; and Kenya: Hassan, Amin S., et al., 'Dynamics and Constraints of Early Infant Diagnosis of HIV Infection in Rural Kenya', *AIDS and Behavior*, vol. 16, no. 1, January 2012, pp. 5–12.
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- 11 United Nations Children's Fund, 'Innovative HIV Point-of-Care (POC) CD4, Early Infant Diagnosis (EID) and Viral Load (VL) Technologies', UNICEF, 2015.
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- 14 Bourne, D.E., et al., 'Emergence of a Peak in Early Infant Mortality due to HIV/AIDS in South Africa', *AIDS*, vol. 23, no. 1, 2009, pp. 101-6.
- 15 World Health Organization, *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection*, 2nd ed., WHO, Geneva, 2016.
- 16 Ford, Nathan, et al., 'The Future Role of CD4 Cell Count for Monitoring Antiretroviral Therapy', *The Lancet Infectious Diseases*, vol. 15, no. 2, February 2015, pp. 241–247.
- 17 High viral load, as per 2016 WHO guidelines, is defined as more than 1,000 copies of the HIV virus in a millilitre of blood.
- 18 Joint United Nations Programme on HIV/AIDS, *Prevention GAP Report*, UNAIDS, Geneva, 2016.
- 19 Jani, Ilesh V., et al., 'Effect of Point-of-Care CD4 Cell Count Tests on Retention of Patients and Rates of Antiretroviral Therapy Initiation in Primary Health Clinics: An observational cohort study', *The Lancet*, vol. 378, no. 9802, 2011, pp. 1572–1579.
- 20 Mazzola, Laura T., and Carmen Pérez-Casas, *Unitaid HIV/AIDS Diagnostics Technology Landscape*, 5th ed., World Health Organization, Geneva, October 2015.
- 21 World Health Organization, *Guidance for Procurement of In Vitro*

- Diagnostics and Related Laboratory Items and Equipment*, WHO, Geneva, 2017.
- 22 Platform sharing refers to the sharing of a single POC device across different health facilities/sites on a predetermined schedule.
 - 23 A 'hub and spoke' model is when a 'hub' site provides the POC testing for neighboring sites/facilities ('spokes') via a limited sample transportation or patient referral network.
 - 24 Consider WHO Guidelines on Post-Market Surveillance of In Vitro Diagnostics: <<http://apps.who.int/iris/bitstream/10665/255576/1/9789241509213-eng.pdf?ua=1>>.
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 - 31 United Nations, *Harmonizing UN Procurement: Common UN procurement at the country level*, High-Level Committee on Management Procurement Network Secretariat, Copenhagen, 2013.
 - 32 World Health Organization, *Guidance for Procurement of In Vitro Diagnostics and Related Laboratory Items and Equipment*, WHO, Geneva, 2017.
 - 33 Within this context, performance refers to verification of the manufacturer's claims by actually testing the device to see how it performs, with consideration of the following: environmental factors (e.g., temperature, humidity, etc.); sensitivity and specificity; turnaround times; and workload and setting.
 - 34 Joint memorandum of understanding among the Global Fund, CHAI, MSF, EGPAF, UNICEF and WHO/Unitaid for EID and viral load testing products 2016.
 - 35 Although logic models vary in format and presentation, they are generally graphical representations or maps which include four key components: inputs (resources); activities; outputs; and outcomes/impact.
 - 36 Refers to test results that fall outside the specifications or acceptance criteria which has have been specified in the official compendia monographs or the finished product specification in registration dossiers.
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