



Federal Ministry of Health

**GUIDELINES
FOR THE IMPLEMENTATION OF
POINT-OF-CARE CD4 TESTING
TECHNOLOGIES IN ETHIOPIA**



Ethiopian Health and Nutrition Research Institute

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Foreword

In resource limited countries such as Ethiopia, inexpensive, accurate, quick, and easy to use laboratory tests and devices are required for the prompt diagnosis and treatment of infectious diseases such as malaria, TB and HIV. Such diagnostics enable immediate initiation of treatment and are crucial for efficient monitoring of efficacy and proper management of patients. Especially in the HIV epidemic, limited access to diagnostic and monitoring tests has been the single most important set-back in the efforts of scaling up access to HIV/AIDS prevention, care and treatment in resource limited settings. The currently available complex diagnostic technologies for virological and immunological tests are expensive; require sophisticated machines and laboratory infrastructure, stable electricity supply, specialized maintenance services and highly trained laboratory personnel.

However, currently, multiple Point-of -Care (POC) reagents and devices that are easy to use with minimal trainings, with stable, ready-to-use reagents, simple, minimal/maintenance-free instrumentations are becoming available. These technologies are primarily meant to improve accessibility of the diagnostics to remote hard-to-reach populations so as to help to quickly diagnose HIV, accurately monitor the disease progression and improve decision making to initiate or monitor treatment. The major advantages of POC reagents and instruments are reduction of turnaround time and thus minimizing patient loss to follow up, increasing number of patients initiating treatment due to same day on-site test results and improving monitoring treatment efficacy. Some of the drawbacks of the POCs as related to their expanded rollout are the low throughput of the devices per day, training, managing the supply chain, implementation of external quality assessment programs due to the large number of testing sites and difficulty of monitoring and evaluation of various data at decentralized sites.

Although there are many POC reagents such as HIV and Malaria Rapid Test kits, recently very few POC CD4 devices have been introduced into the market and more others are in the pipeline. To harness the full benefits of POC technologies, it is imperative that they are

systematically selected, evaluated and introduced for use based on guiding principles that aim at enabling the laboratory system to favorably respond to the demand of the health care services. Selection of new technologies for evaluation should be based on the operational characteristics of each, such as throughput, ease of use, cost etc. and performance characteristics such as accuracy and precision. Therefore, while avoiding monopolies and promoting competition, it is suggested that standardization strategies and guidelines are put in place to limit over-diversification of the devices in use at any one time which may reduce opportunities for bulk discounts.

In Ethiopia, even though there is extensive experience in evaluating and implementing POC reagents for HIV testing, evaluation and adaptation of POC technologies and devices is at an early stage. The recent example is Pima® POC CD4 device that has been evaluated against standard conventional CD4 testing instruments currently in use in Ethiopia, namely, BD FACScout and FACScalibur and produced results that are in agreement with both systems and acceptable for practical purposes. Data from this evaluation study have served as evidence to consider this POC device for potential introduction to appropriately selected health facilities providing ART services and are currently depending on specimen referral system for CD4 testing.

Following the evaluation process, a Consultative Workshop was conducted on March 15, 2012, to discuss and put forward the next steps to implement POC CD4 in particular and POC technology transfer to the Ethiopian national lab system in general. At the Workshop, it was decided that a Task Force, under the leadership of the EHNRI, be established for drafting strategies and guidelines for the implementation of POC technologies. Therefore, these POC CD4 implementation guidelines were prepared by the Task Force as a supplement to the general POC strategy document to serve as detailed guidelines for selection, evaluation, adaptation, implementation and monitoring and evaluation of POC CD4 diagnostics. The document is also intended to be used as a reference for the preparation of product specific

detailed implementation guidelines which will be added as an appendix to this document as they become available in the market and become accepted for use in the country.

The EHNRI believes that these guidelines will help to standardize and ensure the systematic introduction and implementation of POC CD4 technologies in the Ethiopian context. I would like to express my sincere gratitude and appreciation to all who have contributed to the preparation of the document.

Amha Kebede, PHD.

Director General

Ethiopian Health and Nutrition Research Institute

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Acronyms

ANC	Antenatal Clinic
ART	Antiretroviral Therapy
ASLM	African Society for Laboratory Medicine
CDC	Center for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
DOTS	Directly observed therapy, short-course
EHNRI	Ethiopian Health and Nutrition Research Institute
EID	Early Infant Diagnosis of HIV/AIDS
EQA	External Quality Assessment
FEFO	First in, First Out
FMHACA	Food, Medicine, and Health Care Administration and Control Authority
HCT	HIV Counseling and Testing
HCW	Health Care Workers
HIV	Human Immunodeficiency Virus
HMIS	Health Management Information Systems
HR	Human Resource
IPLS	Integrated pharmaceutical logistics system
IQC	Internal Quality Control
LIS	Laboratory Information System
LOA	Level of Agreement
LTFU	Loss to follow-up
M&E	Monitoring and Evaluation
PHSP	Private Health Sector Program
PLWHIV	People Living With HIV/AIDS
PMTCT	Prevention of Mother-to-Child Transmission of HIV/AIDS
POC	Point of Care
QC	Quality Control
SOP	Standard operating procedure
TB	Tuberculosis
TOT	Training of trainers
VCT	Voluntary Counseling and Testing
VL	Viral Load
WHO	World Health Organization

Executive Summary

Ethiopia has introduced and been conducting laboratory testing for over 100 years as the first hospital, Minilik II Hospital, was established in 1906, followed by the Medical Research Institute in 1942 which later evolved into the Ethiopian Health and Nutrition Research Institute (EHNRI). EHNRI has several laboratory technologies capable of testing for a multitude of communicable and non-communicable diseases, such as HIV, tuberculosis, malaria, and other high burden diseases in Ethiopia.

While the HIV prevalence in Ethiopia is relatively low for a Sub-Saharan country at 1.5%, approximately, 800,000 people are living with HIV. Of those, almost 300,000 are currently on antiretroviral therapy. In 2011, almost 10 million people were tested for HIV and received their results. The introduction and expansion of rapid diagnostic testing (RDT) for HIV has allowed for this increased access to diagnostic testing. The WHO 2010 guidelines recommend initiating HIV positive patients on antiretroviral therapy upon a CD4 count of 350 cells/ μ l or WHO stage III or IV. Providing CD4 testing throughout Ethiopia will be essential to initiating additional HIV positive patients on ART and improving overall patient health.

EHNRI conducts approximately 650,000 CD4 test per annum; however, the need for CD4 testing is much greater. In addition to EHNRI, many regional hospitals and laboratories have conventional CD4 testing machines. Though the laboratory network in Ethiopia is extensive and sample referral networks established, the total need for CD4 testing is unfortunately not being met due particularly to challenges with specimen transportation logistics.

Point of Care (POC) testing is a test performed in the immediate vicinity of a patient to provide rapid same-day test results. Such testing will allow for immediate clinical decision-making. In the case of CD4 enumeration, POC testing will facilitate faster initiation on and adjustment of ART. POC CD4 testing has the potential benefit of expanding timely access to testing, increasing timely initiation on ART, providing the correct PMTCT regimen, establishing a baseline

enumeration for patients beginning treatment, and simplifying ART services at the primary care level, and reducing patient loss to follow up. The Implementation Guidelines outlined in this document should serve as a guide to introducing and implementing CD4 POC technologies in Ethiopia.

1. Introduction

Ethiopia has developed a general strategy document for the implementation of Point-of-Care (POC) technologies, and this document is part of the general strategy for the implementation of POC CD4 testing. EHNRI and the Ministry of Health (MOH) will play the leadership roles to execute these guidelines for the implementation of POC CD4 in Ethiopia in collaboration with the Regional Health Bureaus and with the support from HIV care and treatment partners.

POC CD4 testing will be implemented in a phased manner at appropriate facilities. Multiple POC technologies and increased competition in the CD4 market would provide Ethiopia with a variety of options that would best suit the different health care facility needs and reduce costs. POC CD4 technologies will be placed in selected sites based on the established criteria within this guideline.

The Ethiopian POC strategy document incorporates other technologies currently in development that will be considered as they become available, in order to decentralize and create competition in the market for CD4 testing, Early-Infant HIV Diagnosis (EID), HIV Viral Load (VL) testing, tuberculosis (TB) diagnosis, and other infectious and non-infectious diseases and diagnostic tests. The present implementation guidelines will set the standards for POC CD4 testing for the ART program in Ethiopia. Similar guidelines will be developed under the national POC testing strategic framework for effective implementation of new POC testing platforms as they emerge in the market.

In Ethiopia, the volume of patients in chronic HIV care is high with almost 300,000 currently on antiretroviral therapy. The number of HIV positive persons enrolled into ART care in Ethiopia is nearly 3,000 patients per month; however, CD4 testing services that are critical for treatment monitoring and initiation of therapy are not easily accessible. There are challenges in Ethiopia that prevent patients from receiving CD4 testing, such as lack of infrastructure or laboratories at health clinics to support conventional testing, poor service and maintenance of instruments,

reagents requiring cold chain transportation and/or storage, and weak specimen transportation networks. The program needs additional efforts to solve the indicated obstacles. The National Laboratory Master Plan outlines a plan to strengthen specimen referral linkages, contractual maintenance agreements with companies, and decentralization of training of maintenance personnel both on trouble-shooting and preventive maintenance. The implementation of POC CD4 testing will work alongside these efforts and conventional CD4 testing to create a stronger system overall.

1.1 Justification for introducing POC CD4 testing in Ethiopia

Access to CD4 testing remains a barrier to providing effective HIV patient care and treatment in Ethiopia. Some of the key challenges with the current system of conventional laboratory-based CD4 testing include:

- a) **Patient burden** – patients must return to the facility multiple times to receive CD4 results. This places a high burden on patients, and it can adversely affect effective management of patients on treatment and delay in initiation of treatment and cause patient loss-to-follow-up.
- b) **Specimen referral** – because most health centers providing HIV care do not conduct CD4 testing, most refer specimens to a conventional laboratory for testing. This often requires complex logistics and transport conditions may compromise specimen quality in addition to the usually long turn-around-times. If specimens can only be referred on certain days, this limits access to testing.
- c) **Staff requirements** – conventional CD4 technologies must be used by a highly skilled technician and require extensive training to run; this means they cannot be used in many facilities without highly trained staff, and staff re-locations are a major concern.
- d) **Cold chain** – The transport of many reagents in the current system requires cold chain; if this is not maintained, accuracy of results may be complicated. Additionally, maintaining the cold chain is difficult given infrastructure constraints
- e) **Service and maintenance** – A robust system for the provision of regular preventive and efficient curative maintenance services are crucial for uninterrupted functioning of

conventional laboratory testing equipment platforms. Underdeveloped capacity, lack of spare parts and logistic problems are currently posing immense challenges to Ethiopia's laboratory equipment maintenance program across all conventional testing instruments currently in use in the country. Introduction of cost-effective POC technologies with minimal or no maintenance needs and spare part requirements is one of the options to minimize the frequency of service interruptions due to failures and prolonged down-times of conventional testing systems. As such, consideration of POC technologies for CD4 testing services is of particular importance as this parameter provides critical information for the proper management of patients on treatment and prompt initiation of therapy for those who are in need.

Introducing POC CD4 diagnostics can expand access to critical CD4 testing, allow patients to receive results on-site the same day they are tested, and it can reduce the logistical challenges of specimen transportation. Some of the key potential benefits of POC CD4 testing are:

- a) **Expand timely access to CD4 testing** – 24 percent of health facilities providing ART in Ethiopia had conventional CD4 diagnostic machines by mid-2011 and only these facilities can provide same day results; even with specimen referral networks, this limits patient access to CD4 testing. Conventional CD4 testing through specimen referral requires patients return to the facility to receive their results; however, with POC CD4 testing, patients can receive results on-site the same day they are tested.
- b) **Increase timely initiation on ART** – POC CD4 testing will help identify PLWHIV in WHO clinical stages 1 and 2 who are eligible for ART. Access to a CD4 count is important to start ART early, i.e. before the patient is too sick. Earlier or so-called “upstream” ART access may reduce individual morbidity and mortality, mother-to-child transmission of HIV and the incidence of HIV-associated tuberculosis (TB). A recent study (Severe et al. 2010) showed a 75% reduction in mortality and a 50% reduction in TB incidence associated with starting ART earlier. With POC testing, clinicians can immediately use test results to drive treatment decisions.

- c) **Provide the correct PMTCT regimen in a timely manner** –with a CD4 count, PMTCT sites will be able to implement early initiation (at 14 weeks) with the appropriate WHO PMTCT regimen. With full implementation of PMTCT option B+, it will serve as an important baseline test.
- d) **Establish a baseline for patients beginning treatment** – patients need a CD4 test as they are initiating antiretroviral therapy to help monitor their response to treatment and drug adherence.
- e) **Simplify ART at the primary care level and de-centralize care** – POC CD4 testing will reduce dependence on clinical acumen and the need for WHO staging. This will increase the decision-making power and numbers initiated on ART by nurses and other health care workers and will reduce the loss-to-follow-up.
- f) **Reduce patient loss-to-follow-up** – reduced visits and waiting time for patients before they can initiate ART can help reduce patient loss (Jani et al 2011) and reduce the patient burden of time and travel to receive care.

1.2 Definition of a POC CD4 technology

A “Point of Care” (POC) CD4 test is a CD4 test performed in the immediate vicinity of a patient to provide a rapid same-day result outside the conventional laboratory environment, in order to facilitate immediate clinical decision-making, including initiation and adjustment of anti-retroviral therapy.

Essential criteria that best define ‘Point of Care’ technologies are:

- Patient Impact
 - Same-day on-site test results
- Short turn-around time (no more than 20-30 minutes)
- Ease of Use
 - Easy to use for non-laboratory personnel
 - Highly automated with minimal manual steps

- No precise sample measurement or manipulation required
- Simple sample collection – use of capillary blood will be preferable so that phlebotomists are not required to operate the device
- Results are easy to read
- Deployment
 - Consistent electricity and refrigeration not required – device can operate on battery power or an alternate power source
 - Portable equipment with no manufacturer or specialized installation required
 - Long shelf life for consumables (at least 6 months once consumables reach facility though preferably longer)
 - Material waste can be disposed of safely
- Quality Control
 - Internal QC mechanisms available
 - Compatible with External Quality Assurance (EQA) schemes
- Cost
 - Similar in cost to conventional testing methods
 - Equipment and consumables cheap enough for deployment at low volume sites

Ethiopia will use these essential POC criteria to determine which potential technologies fit this definition and exclude technologies that fail to meet these criteria. Ethiopia will reserve the right to use evaluation results from other countries of similar conditions for those products that it determines to have the most potential for implementation, according to this definition of POC.

This definition can cover devices or device-free systems including:

- a) Non-instrumental systems** include disposable systems or devices that vary from reagent test strips for a single test to sophisticated multi-analyte reagent strips incorporating procedural controls
- b) Small or desktop analyzers:** usually handheld or small devices that may differ by size and type

1.3 Regulation of POC CD4 technologies

EHNRI will support the regulatory processes of POC technologies in terms of selection, evaluation, implementation, overall quality assurance and monitoring and evaluation of their performances. FMHACA will follow its own procedures to register new technologies but EHNRI, based on established criteria, will select technologies with no requirement for prior registration by FMHACA for evaluation purposes. However, if after evaluation, the technologies are recommended for use in laboratories and health care facilities in Ethiopia, FMHACA's registration is required before they are implemented. Where appropriate, EHNRI can also use evaluation results from accredited laboratories or institutions outside Ethiopia or ASLM collaborating centers to recommend technologies rather than conducting an in-country evaluation. Doing so will reduce the costs and resources of conducting an additional evaluation and speed up the introduction of new technologies.

Following the completion of an evaluation, EHNRI will submit a report and implementation guidelines to the Ministry of Health. In introducing the POC technologies, partners and health care facilities should follow these guidelines in consultation with EHNRI. Should a technology already registered not pass evaluation or not be recommended by EHNRI, FMHACA can revoke registration and prevent the technology from being imported.

2. POC CD4 Site Selection

To ensure that appropriate sites are selected for POC CD4 testing, a robust site-selection process is required among government and stakeholders. A process that effectively maps and prioritizes health facilities for adoption of new POC CD4 technologies is required to ensure maximum impact on the greatest number of patients.

Process for conducting site selection:

- A leadership team from EHNRI and programs at MOH in collaboration with partners will conduct a mapping exercise of all health facilities with active ART/PMTCT/VCT sites. This mapping exercise will consider the different POC CD4 technologies best suited for the various health facility types and/or patient numbers. Private clinics should be included as part of this mapping exercise if they are considered as ART/PMTCT/VCT sites and have an arrangement with the MOH.
- The team will identify sites that qualify for the POC CD4 technology that is being introduced using the site selection criteria (below) and will prioritize sites.
- The team will allocate the POC CD4 devices or technologies available and produce the site selection list.

POC CD4 testing is not ideal for every site, and is not meant to replace conventional testing or the existing laboratory infrastructure. It is important to recognize that different POC CD4 devices will be optimal for different settings, and therefore clear site selection criteria are needed. Maximizing patient impact should be the guiding principle for introduction and site deployment of these devices. As such, the following pre-defined site characteristics should be evaluated during the site selection process.

2.1 Site selection criteria

Facilities that do not have conventional CD4 diagnostic technologies on-site will be prioritized to receive POC CD4 technologies. Other key factors that will drive prioritization:

- a) Patient volume** (actual or expected): patient need and demand will be measured for each facility based on the number of patients requiring CD4 testing, or number of patients enrolled in pre-ART and ART care. Non-ART sites may also be considered for placement of CD4 technologies.
- b) Current access to CD4 testing:** introducing a POC CD4 technology will have more impact at a facility with no access to CD4 testing than at one with strong access to

testing through sample referral; therefore, accessibility of and distance to conventional CD4 testing should impact prioritization.

High-burden facilities with a conventional diagnostic may be considered to receive a POC CD4 technology at a particular entry point, for example in the ANC or VCT. POC technologies are not recommended for use as back-up devices for conventional CD4 machines. This would add unnecessary complications as it would require creating a back-up supply chain system and training additional operators. Additionally, POC technologies rarely have similar through puts and therefore would not fulfill the testing volumes of conventional machines. Instead, sample referral networks and improved service and maintenance should be the solutions if conventional devices break down.

3. Training and use of POC Technologies

Upon introduction in a facility, staff at the facility should be trained on the technical use of the POC technology as well as integration of the technology into facility systems. Strong technical training is important to ensure accuracy of results and to keep error rates low. Systems integration training will help facilities maximize utilization of the technology and patient impact.

EHNRI and the MOH will work to incorporate POC technology training into pre-service training in the future as this may be a more sustainable and cost-effective training method.

3.1 Training of Trainers (TOT)

The training of trainers will bring together representatives from EHNRI, partners, regions, and the manufacturer of the technology. The aim of the TOT is to prepare a cadre of master trainers to train facilities on technical and systems considerations. The training will cover all technical and systems Standard Operating Procedures (SOPs) for POC CD4 testing that facilities will need to implement.

3.2 Facility Trainings

EHNRI, partners, and regional representatives will coordinate facility trainings. These trainings will generally occur on-site, and they will cover both technical and systems training. Master trainers trained through the training of trainers will conduct the end-user facility trainings.

4. Quality Assurance

A comprehensive quality assurance program will be very important to ensure accuracy of results in a decentralized laboratory system. Systems to ensure the maintenance of an adequate level of quality will include:

Internal quality control:

- All POC technologies introduced in Ethiopia should have internal quality control mechanisms
- Facilities should run internal quality controls regularly in accordance with manufacturer guidelines and recommendations.

External Quality Assessment (EQA):

- All POC technologies introduced in Ethiopia should be compatible with External Quality Assessment (EQA) schemes

Supportive Supervision:

- Master trainers should monitor operators' use of POC technologies and sample collection techniques through supportive supervision

Inter-laboratory comparison schemes:

- Sites can exchange samples among each other to check the quality of testing and the overall performance of technologies as coordinated by regional laboratories
- In the unexpected absence of EQA programs, a system for inter-laboratory comparison will be very important.

5. Monitoring and Evaluation

EHNRI will establish a standard POC CD4 test monitoring system, testing registers and monthly reporting forms. The M&E system will support POC CD4 testing implementation, access to patients and logistical capacity and performance. Regions must ensure that reporting materials, tools and systems follow national standards in support of the M&E system and are technology neutral.

The main goals of introducing POC CD4 testing in Ethiopia are to increase timely uptake of CD4 testing, increase timely receipt of CD4 test results, and to improve and accelerate ART initiation of eligible patients. A Monitoring & Evaluation (M&E) plan will be implemented to measure the scale-up of this program, and to assess the impact of this program in achieving these goals. EHNRI will design the indicators used in M&E for POC CD4. Some of these may include:

5.1 Program Scale-up: To measure the goals of scaling up POC CD4 testing in public health facilities in Ethiopia, targets should be set for some or all of the following indicators:

- Number of sites trained to perform POC CD4 testing; number of healthcare workers trained and certified to perform POC CD4 testing;
- Number of sites successfully passing External Quality Assessment (EQA) for POC CD4 testing;
- Number of total POC CD4 tests performed.

5.2 Impact Assessment: As this program is expected to generate significant patient benefits, separate indicators will be used to measure the impact that POC CD4 testing has on patient outcomes. These indicators will be measured through the national HMIS and through data collected from POC connectivity.

Metrics collected through connectivity will include:

- Number of patients receiving a CD4 test
- Average patient CD4 count
- Error rate of each facility and operator

Metrics collected through HMIS will include:

- Current patient enrollment numbers on ART
- New patients initiated on ART
- Number of patients ever initiated on ART

As needed or desired, EHNRI or partners may undertake additional impact assessments.

6. Data management

As CD4 testing is decentralized to lower levels of healthcare facilities within Ethiopia, it is important that systems are developed to monitor the data generated by this new method of testing. Data management systems will be developed at the site and national level. Data management systems will, therefore, be put in place at the following levels:

6.1 Site Level Data Management: To ensure that POC CD4 testing achieves its intended purpose of accelerating eligible patients into care and treatment, systems will be developed to ensure effective management of patient testing data at the site level. These systems will dictate how POC CD4 results flow from the healthcare worker who performs POC CD4 testing to the patient and how results are recorded into health facility logbooks and the patient's file. Careful attention must be taken to ensure that every POC CD4 test result is received by the patient and provided to a clinician in a timely manner so that clinical decisions can be made based on these results. The impact of POC testing on patient outcomes relies on effective data management systems to minimize opportunities for lost test results and accelerate the interpretation of results. Site level data management will be covered in both the TOT and the site operator training modules.

6.2 National and Regional Level Data Management: There is also need to develop systems for ensuring that data from POC CD4 testing at the site level feeds into the national and regional databases for CD4 testing. Unlike conventional CD4 testing that utilizes national specimen transportation networks for data flow from health facilities to the regional and central levels; all data for POC CD4 are based at the site level. Systems for data flow to the regional and central levels to ensure appropriate program management and monitoring of testing should be developed. These systems should be disseminated at the site level during training, and program managers at the regional and central levels should put SOPs in place to ensure complete and efficient data flow. These SOPs should specify how often data should be collected at both levels and entered into the regional and national databases and how quality control of the data should be conducted.

6.3 Mobile Technology Data Management: Because CD4 testing data will need to be collected from a larger number of testing sites over which EHNRI and/or the Regional Labs may not have direct oversight, using a paper-based system for collecting data may be a challenge. To address this issue, it is possible to use mobile technology to transmit and analyze the data that is stored automatically on each POC CD4 device. The operator can transmit testing data periodically (e.g. after each day of testing) to the regional and central databases residing at the Regional Labs and EHNRI, respectively, and which can be linked to a national laboratory information system (LIS). This data can then be synthesized into reports to monitor the progress of the POC CD4 testing program. These reports will help inform areas such as supply chain (by measuring the number of tests conducted at each site), quality assurance (by assessing whether each site is running and passing its daily quality controls), and service and maintenance (by assessing whether each instrument is functional). Additionally, once the LIS is operational this system can be used to track individual patient data, such as a patient's CD4 count history over time, and improve national HIV surveillance and monitoring of epidemiological trends. This system of data transmission should be implemented at the same time as the devices are

distributed. EHNRI will also work with other diagnostics suppliers to ensure that this functionality becomes standard with new POC technologies as they become available.

7. POC CD4 Product Selection and Adoption for Use

As detailed in the national POC strategy document, as new POC diagnostics become available, competition should be encouraged to ensure that Ethiopia does not become overly reliant on a single supplier for any one test and that multiple products are used that meet the needs of different types of settings. At the same time, it is important to maintain some standardization of equipment in order to avoid excessive complication of the supply chain. For example, in the POC CD4 product class, there are several products available and in development that have clear advantages and disadvantages for different types of facilities. One product may be ideal for higher volume health center settings, while another product may be ideal for sites with lower volumes and without consistent electricity. For CD4 testing, Ethiopia's goal will be to evaluate several products or review external evaluations and approve a limited number to adopt across different levels of the healthcare system, in order to provide the greatest patient impact and the most efficient and cost-effective provision of services. The number of products approved for use will need to be limited in order to minimize the cost and complexity of managing supply chain, service and maintenance, training, and monitoring and evaluation for a large number of testing sites. Implementation will be conducted in a phased manner at facilities where the technology is well suited. This strategy will ensure that there is immediate patient impact achieved from the currently available technologies, while allowing for new, more suitable technologies to be adopted as they become available.

Currently there are several POC CD4 technologies in the pipeline among which three are available in the market; PointCare NOW™, the Pima™ CD4 Analyzer and the CyFlow™ CD4 miniPOC. These POC technologies have different device characteristics in terms of cost, throughput, ease of use etc. which are shown in Table 1. Due to the differences in throughput;

these devices are adapted to different levels of health facilities providing ART services. Among the three, the Pima CD4 analyzer has been recommended for use by WHO and evaluated in Ethiopia and produced results that are in agreement with the conventional techniques. Data from this evaluation study have served as evidence to consider this POC device for introduction to appropriately selected health facilities which are currently depending on specimen referral system for CD4 testing. Thus in the appendix section, detailed Pima implementation guidelines have been added (see Appendix 1). In the event that Ethiopia decides to adopt the other two technologies or any other technology in the pipeline which becomes available in the market, based on the criteria specified in the national strategy document, detailed product specific implementation guidelines will be developed and added as appendices to this document.

Table 1: Product Characteristics of 3 Point of Care CD4 devices currently available in the market

Product	Pima™ CD4 Analyzer	PointCare NOW™	CyFlow™ CD4 miniPOC
Same day on site test result	20 tests/day	50 tests/day	250 tests/day
TAT	20 minutes	8 minutes	>30 minutes
Ease of use	No manipulation	No manipulation	Needs manipulation
Device cost	6000-12000USD/device	25,000USD/device	Approximately 9380USD/device
Reagent cost	6-12USD/test	10USD/test	3.96USD/test
Pre-qualification/peer review/independent performance evaluation	WHO prequalified, five independent performance evaluations, CE marked	FDA approved, no WHO prequalification or independent performance evaluation	??

8. APPENDICES

Appendix 1- Pima® POC CD4 TESTING DEVICE IMPLEMENTATION GUIDELINES

These guidelines will provide specific guidance for the introduction of the Pima® POC CD4 Analyzer. All guidance laid out in the generic POC CD4 guidelines should be applied to the implementation of Pima® devices.

The Pima® device is a POC device that produces absolute CD4 counts from 25 µl of blood in twenty minutes. The device can run up to twenty tests per day depending on operating hours of the health center. All reagents are sealed in a disposable test cartridge, and no external calibration or regular maintenance is required. The device operates on an external power source or a rechargeable battery. Additionally, the Pima® machine stores all results in a data archive which can be downloaded or printed after the tests have been performed. The Pima® POC CD4 Analyzer has been successfully evaluated by the EHNRI. The evaluation indicated that Pima® performed well compared to the BD FACScount and FACScalibur conventional CD4 testing systems currently in use in Ethiopia.

Site selection

Classification of health facilities by volume for Pima®

Patient volume is one of the major criteria for site selection for the implementation of Pima POC CD4 testing for initiation of ART and/or ART monitoring. The health institutions are, therefore, classified into three categories according to the number of patients they serve for CD4 testing.

Low level CD4 testing sites (1-5 patients per day)

In these sites, the number of patients requiring CD4 testing is estimated to be 1-5 patients per day. These sites are currently using the referral linkage system and the results are obtained in a minimum of one week. A total of 5-25 patients require CD4 testing in these health institutions per week. Since the number of patients is small, a weekly referral system should continue to be used for CD4 testing. For those sites that are very far from the reference labs and have poor sample transportation systems, placing a Pima® device to serve a group of low-volume sites may be considered. The site receiving a device will serve as a referral lab for other low volume sites around it that can send samples or refer patients. This will be a cost effective solution until simpler, inexpensive POC CD4 technologies are available.

Medium level CD4 testing sites (6-20 patients per day)

In these sites, the number of patients requiring CD4 testing is estimated to be 6-20 patients per day. Approximately, 30 to 100 patients require CD4 testing per week and currently a referral linkage system is used. Taking the throughput and the cost effectiveness into consideration, the Pima® device is the most adapted method of CD4 testing for this level of site as the turn-around-time to results will decrease and maximal patient impact will be attained as compared to conventional CD4 testing through sample referral.

High level CD4 testing sites (21-50 patients per day)

In this group of health facilities, the number of patients requiring CD4 testing is estimated to be 21-50 patients per day and 105-250 per week. In these health institutions, the number of patients to be monitored and initiated on ART is high; therefore, there is a need for on-site testing. The choice of a POC technology should, however, be balanced depending on the availability of a high throughput technology, equipment cost, cost per test, and infrastructure requirements. Placing two Pima® devices or one high throughput POC CD4 technology, if and

when available, will be considered. For facilities that have high patient volumes beyond the capacity of Pima® devices and fulfill the necessary infrastructure requirements, conventional CD4 machines will be considered. If facilities receive a POC CD4 technology that cannot handle the volume of patient testing required, a referral system should be maintained to complement the POC testing.

Based on the above criterion, Pima® devices will be prioritized for placement in medium-level CD4 testing sites or, where applicable, networks of low-level CD4 testing sites in hard-to-reach areas.

Basic requirements for site selection:

Sites not meeting the basic requirements will not receive a Pima® device. These basic requirements are:

- Infrastructure: the facility should have at least intermittent electricity to charge the device;
- Treatment: at this time, only facilities providing ART services on-site will be eligible to receive a Pima® device;
- Staffing: a facility should have at least one full-time trained laboratory personnel or other healthcare worker to oversee operation of the device.

Due to infrastructure considerations, health posts are not eligible to receive a Pima® device.

Factors for prioritization:

Facilities will be prioritized based on the following parameters. The highest priority facilities, as determined by the site selection exercise, will be the first to be allocated a device (in accordance with a phased regional rollout).

- Patient numbers – within the category of medium-level CD4 testing sites, facilities with higher patient volumes should be prioritized to receive Pima® devices;
- Current patient access to CD4 testing;

- Facilities that already have a conventional CD4 diagnostic should not receive a Pima® device unless the device is for use in a specific entry point, for example in the VCT or ANC;
- Facilities that have chemistry and hematology analyzers should be prioritized to increase the number of facilities that can provide a full package of HIV diagnostic, staging and treatment monitoring services.

Adjustment with the referral linkage

Ethiopia has a well-established sample referral system where more than 500 health facilities refer samples to higher-level facilities for CD4 monitoring on conventional CD4 machines. With the placement of Pima® devices or any other POC technology, there is a need to revise the sample referral network. This will require adjustment of logistics for reagents and consumables. If any facility receiving a Pima® device has patient CD4 testing volumes higher than can be handled by a Pima® device, sample referral linkages should be maintained to ensure all patients are able to receive CD4 test results. As mentioned above, some low-volume sites receiving a Pima® POC CD4 device can serve as testing sites for additional facilities nearby with no or poor access to conventional CD4 testing, as outlined in Figure 1.

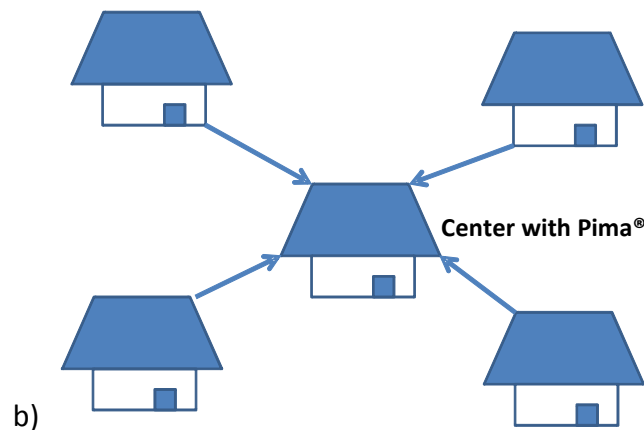


Figure1. Schematic representation of the possible sample referral linkage for Pima® devices among several low CD4 test volume facilities.

Procurement Process

EHNRI will provide guidance for the overall implementation of Pima® POC CD4 testing in collaboration with the Pharmaceutical Fund and Supply Agency (PFSA). Device placement decisions should be made in accordance with EHNRI's site selection/prioritization list and should be timed according to the phased rollout of the technology. For device procurement by partner organizations specifically for government owned health facilities procurement should happen in consultation with EHNRI and in addition, the following details must be provided to EHNRI/Regional Laboratories at the Regional Health Bureaus at the time of its placement to avoid duplication, ensure the reagent supply availability and the smooth implementation of the technology:

- Number of Pima® devices to be procured
- Serial number of each Pima® device
- Date of installation at each facility
- Expected patient volumes at each potential facility
- Proposed training schedule and plan
- Contact information for laboratory personnel or on-site focal person

At the time of device placement, partners should ensure there is full coordination with PFSA, which will allow for ongoing supply of reagents to each facility receiving a device.

An efficient distribution system is critical to respond to the supplies needs at individual sites. Scheduled distribution of supplies and reagents to health facilities will be maintained. For this, forecasting for reagents for each of the Pima® devices will be conducted based on the test volumes expected from the number of patients that are currently on ART and in pre-ART care in the selected sites, the expected number of newly identified HIV individuals requiring a CD4 test, and the current CD4 sample referral volumes. Additionally, data acquired from each Pima® device through connectivity can be used to assist with reagent forecasting. Forecasts will be updated at regular intervals by PFSA and commodities will be ordered from the supplier and

distributed by PFSA on a regular basis according to the existing system and according to orders placed by facilities.

In order to place a Pima® device at a facility, it is critical that partners have the full approval of the MOH and EHNRI and follow the guidelines for site selection prioritization outlined in this document.

Distribution

The following recommendations exist for efficient distribution of the Pima® devices. Equipment and supplies should be delivered to the facility at the same time that on-site facility training occurs to ensure that machines are not used by untrained staff and that trainees can immediately apply lessons learnt. Each facility receiving a Pima® device should receive the following items during the initial delivery/installation that will occur concurrently with on-site training:

1. One Pima® POC CD4 Analyzer with its printer and bag
2. A total of 500 reagent cartridges as the initial allocation. The expiry date should be for a minimum of six months after the device reaches the facility
3. One normal bead standard and one low bead standard (these will expire six months after first use)
4. A total of 10 rolls of thermal paper for printing assuming that one roll of thermal paper can be used for 50 patients
5. One flash disk to store the data as a back up

Any facility designated as a priority higher-volume facility to receive two Pima® devices should receive the following items in the initial allocation:

1. Two Pima® POC CD4 Analyzers with two printers and two bags
2. A total of 1000 reagent cartridges expiring no sooner than six months after they reach the facility

3. Two normal bead standards and two low bead standards(these will expire six months after first use)
4. 20 rolls of thermal paper
5. One flash disk

Service and Maintenance

Before procurement of the machines, it is important to agree with the vendor on the maintenance terms. These terms may include device swap-out service, device warranties, and device leasing options. Alere operates under a “swap-out” model in the event that a device is broken; it is important that swap-out Pima® devices be made available in the regions and are not only stored centrally. EHNRI will make negotiations with the vendor on the maintenance terms and conditions which should include but not limited to specifications for response time for remedial actions, in-country responsible entities for these actions both at the regional and central levels, number of reserve devices and storage locations, communication network and mechanisms, duration and pricing of the agreement. EHNRI may opt for negotiation with the vendor on the possibility of leasing the equipment taking the national regulation governing this transaction into account, and this will be further communicated with PFSA for implementation.

Training

EHNRI and the MOH will coordinate training on use of Pima® devices. Trainings will include both technical and systems training and will require the support of the manufacturer and partners.

Training of Trainers

A standardized technical training will be given to the National groups from EHNRI and representatives from regional laboratories by Alere during the TOT. This training will include details on operation of the device, correct sample collection method, trouble shooting, and coordination of repairs and swap-out. EHNRI and MOH will lead systems training for all master

trainers. This training will cover the required facility changes necessary for patient flow, documentation practices, and referral to testing.

On-site facility trainings

The EHNRI, regional representatives and partners will work to coordinate on-site trainings at all facilities receiving a Pima® device. Master trainers will be responsible for conducting the trainings in accordance with the plan and curriculum provided by EHNRI.

Facility trainings will be conducted according to the following guidelines:

- Facility trainings will be on-site and will occur over 2 days
- Facility trainings will occur at the same time as placement of the Pima® device with adequate reagents and specimen collection supplies at the facility
- The aim of trainings will be to ensure all facilities follow technical and systems SOPs as established by the manufacturer and EHNRI
- At least two (and generally three or more) operators at each facility will be trained on technical operation of the device. These operators will need to be certified according to the standards outlined in 'Operator Certification'.
- Facility leadership and key staff will be brought together for a systems training. This training should include the facility director, the clinician responsible for ART initiation, laboratory personnel, key ART nurses, and the Pima® operators. Systems training will include elements including but not limited to:
 - Adjustment of patient flow to ensure patients receive same-day test results and device utilization is maximized
 - Data management – ensuring all patient results are recorded
 - Sustainability – managing stock, ordering for new supplies, and coordinating repairs
- During the first day of training, the trainer will cover the key technical and systems curriculum, and during the second day the trainer will work with facility staff to implement the lessons learnt
- The device manufacturer will provide all technical training materials and job aides

- EHNRI and the MOH, in coordination with the Regional Health Bureaus, will provide systems training materials and job aides
- In the initial implementation phase and until subsequent evaluations of device field performance and personnel competency indicate otherwise, Pima® devices will be placed in laboratories of health care facilities. In large facilities, however, they may be placed in VCT settings.

Operator certification

At the end of the on-site training, trained health facility staff will undergo a certification process to determine their competency to provide Pima® CD4 testing. This will include certification of each individual who will conduct testing, as well as certification of the operating environment to determine its fitness for Pima® CD4 testing. This may consist of each operator performing the test under direct supervision in order to observe that the sample collection and testing procedure are correct. No operator will be permitted to give Pima®-generated CD4 results to patients until this certification process is complete. In the case that an operator does not perform adequately during the certification process, this can be addressed with re-training.

Quality assurance

Quality assurance program for the Pima® POC CD4 machine will use the following strategy:

1. Internal control materials: once opened, the internal quality control materials can be used for six months. Laboratories will use these controls by running the normal and low beads once daily before the operator begins running samples on the machine.
2. External quality assessment: the Pima® POC CD4 device is compatible with the EQA scheme established by the national laboratory system at the EHNRI. All facilities receiving a Pima® device will be enrolled in the national EQA program.
3. Strong supportive supervision: device operators' use of the equipment and sample collection technique should be monitored through scheduled supervision by the regional and sub-regional laboratories and regional hospitals (for those regions that

do have regional laboratories). Master trainers should conduct the supportive supervision visits.

4. Inter-laboratory comparison schemes: since Pima® CD4 devices will be more than one per Woreda or even per city, facilities may exchange samples to check the quality of results and the performance of instruments. This exercise or system should be coordinated by the Regional Laboratories. In the unexpected absence of EQA programs, a system for inter-laboratory comparison will be very important.

Connectivity of Pima® CD4 devices

Modems will be purchased through Alere for the Pima® devices and connected to each device by USB. The operator can transmit testing data periodically (e.g. after each day of testing) to regional and central databases residing at the Regional Labs and the EHNRI, respectively, which can be linked to a national laboratory information system (LIS). These data which also include data on internal quality control can then be synthesized into reports to monitor the progress of the POC CD4 testing program. These reports will help inform areas such as supply chain (by measuring the number of tests conducted at each site), quality assurance (by assessing whether each site is running and passing its daily quality controls), and service and maintenance (by assessing whether each instrument is functional). Additionally, once the LIS is operational, this system can be used to track individual patient data, such as a patient's CD4 count history over time, and improve national HIV surveillance and monitoring of epidemiological trends. This system of data transmission should be implemented at the same time as the devices are distributed.

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