Background: Current EID Programs and the Introduction of POC EID

Despite the reduction in rates of mother-to-child transmission of HIV, there are still over 400 infants born with HIV every day.[1] Globally, 220,000 new pediatric HIV infections occur each year, with 130,000 child deaths due to AIDS. Without treatment, up to 30% of infected children will die by their first birthday, and 50% by their second[2]. Peak mortality for infants born with HIV occurs between 2 and 3 months of age[3]. Early Infant Diagnosis (EID) is a gateway to care and treatment for HIV-exposed infants up to 18 months. WHO recommends that all HIV-exposed infants receive a virological test within 2 months of birth, and recently added a recommendation for at- or near-birth testing.

Access to EID using conventional lab-based platforms has improved in recent years. Coverage increased from 28% in 2011[4] to 50% in 2014[5]. However, 43% of EID test results are never received by caregivers or patients[6,7,8,9] and only 31% of HIV-positive children (0-15 years) accessed treatment in 2014[10]. Urgent efforts are needed to improve health outcomes of HIV-exposed and -infected children.

Several Point-of-Care (POC) EID technologies are now available which can address the gaps left by conventional testing and help to optimize national EID programs. Three POC EID assays have received CE-IVD approval (Alere Q, Cepheid GeneXpert, and Diagnostics for the Real World SAMBA), two of which are also WHO Prequalified (Alere Q and Cepheid GeneXpert). POC EID has been shown to significantly reduce turnaround times and increase treatment initiation rates[11,12] – especially critical within the peak mortality period. Recognizing the potential impact of these new devices, the WHO recommended the use of POC EID in its 2016 guidelines.

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[1] Children and HIV fact sheet. UNAIDS. July 2016. http://www.unaids.org/sites/default/files/media_asset/FactSheet_Children_en.pdf

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[5] HIV Treatment and care fact sheet: What's new in infant diagnosis. WHO, November 2015. http://www.who.int/hiv/pub/arv/arv2015-infant-diagnosis-factsheet/en/

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[10] UNAIDS/UNICEF/WHO Global AIDS Response Progress Reporting and UNAIDS 2014 HIV and AIDS estimates, July 2015

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Compared to lab-based testing, POC testing significantly reduced delays across the EID testing and treatment cascade, enabled same-day receipt of test results and same-day initiation of ART for HIV-positive infants, and improved the rates of ART initiation to about 90% (Table 1). Additionally, in Mozambique, although retention of infants can still be improved, POC testing improved infant retention by 18.7% (Table 1). Malawi assessed HIV positivity rates across different settings and determined that access to POC enabled testing within hospital pediatric wards, where ~25% of infants tested were HIV positive (46% at inpatient and 11% at outpatient, compared to the study average of 5.3%). Both studies found POC testing could be accurately performed by non-lab staff.

	Mozambique		Malawi	
	SOC[1]	POC[2]	SOC[1]	POC[2]
TAT between sample collection and results received (days)	125	0	56	0
TAT between sample collection and ART initiation (days)	127	0	38	0
Proportion of HIV-positive patients initiating ART (%)	12.8	89.7	51.6	91.1
Patient retention rate 3 months after ART initiation (%)	42.9	61.6	n/a	n/a

Table 1. *Effect of POC Testing on Patient Outcomes*

In spite of the transformative patient impact achieved by POC EID, scaling up access to POC nucleic acid amplification testing (NAT) technologies in a decentralized program will raise a number of programmatic challenges and risks that will need to be managed and mitigated. Decentralization will increase the need for improved forecasting and supply-chain management, service and maintenance provision, end-user training, and quality assurance. Addressing these issues with adequate resources dedicated to quality assurance will be critical to ensuring that POC NAT testing networks operate at their full potential, ensuring that patients receive accurate same-day test results every time.

Quality Assurance

Both quality assurance and quality control are meant to ensure the accuracy and precision of the results produced by diagnostic testing. External quality assurance (EQA) is a management plan, process, or system to ensure the quality and integrity of diagnostic testing and subsequent data, while internal quality control (IQC) is a series of analytical process measurements used to assess the quality of each diagnostic test and subsequent test result. Consistent monitoring of both quality assurance and quality control will result in correct and reliable diagnostic test results for patients, allow for immediate corrective action if problems arise, and minimize the downtime of technologies needing repair.
For further technical information on Quality Assurance, please refer to “Improving the quality of HIV-related point-of-care testing: ensuring the reliability and accuracy of test results.” Additionally, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has conducted an analysis of available quality

assurance methods for POC technologies. Please refer to Jeff Lemaire (jlemaire@pedaids.org) for further information.

Purpose of the Quality Assurance Budgeting Tool

The Quality Assurance Budgeting Tool is intended provide a resource for programs with an existing quality management plan and/or quality assurance mechanism that are adding a new technology such as POC CD4 or NAT testing to a conventional testing network. The tool assumes that some components of an existing testing network, including program management, staffing, and trained professionals already exist, however there would still be an incremental cost to adding new technologies, including providing additional training, purchasing materials, transportation, and corrective actions. With this context program managers will find this tool useful for budgeting the marginal cost of providing quality assurance for new devices that have recently been added or are planned to be added. It is important to draw the distinction between this budgeting tool and more comprehensive costing tools that might provide a somewhat different result.

The London School of Hygiene and Tropical Medicine (LSHTM) and International Diagnostics Center (IDC) have created a costing tool that includes both the economic and financial incremental costs of starting and operating a POC EQA program. This includes the start-up costs, such capital investments (laboratory infrastructure, vehicles, etc.) and training. This comprehensive approach provides the user with an overall cost approximation for long-range planning, treasury/donor budgeting, and other analysis, i.e. CEA, including academic publication.

The CHAI-developed Quality Assurance Budgeting Tool is a budgeting tool which includes the incremental costs of adding an EQA and other QA methods for new devices to an existing quality assurance program, assuming that laboratory equipment, national staffing, and vehicles are already provided. The tool focuses on the annual cost for operating such a program, including provisions for materials, transportation, and human resources. It is intended to provide program directors or managers with a tool to assist with understanding the costs they can expect to incur from introducing EQA and QA to their POC programs.

The tool includes multiple approaches to quality assurance, including internal quality assurance (controls), mentorship, proficiency testing, duplicate testing of specimens, remote monitoring via connectivity, and paper and e-module-based testing approaches. An integrated quality assurance program will use multiple methods to provide comprehensive monitoring of all aspects of testing and provide checks with enough frequency to provide prompt corrective action, thereby preventing incorrect test results from being delivered to patients. The tool is designed to be flexible so that program managers can select the approaches consistent with national guidelines and robust quality assurance mechanisms.

Using the Quality Assurance Budgeting Tool

Implementing the tool requires accurate data reflective of the national context in which it is being implemented. Gathering the necessary information will likely require referring to multiple sources within the national program and, at times, to international references when data is not available in-country. The strength of the data entered in the tool will determine the robustness of the outputs so it is important that the necessary time and resources are dedicated to gathering this information prior to reviewing outputs from the tool. Examples of necessary data include number of additional devices enrolled, the costs to run mentorship and training activities, facility issue rates, and number of corrective action visits required. Some of these may be estimates that will evolve over time. The tool can be revisited as the program develops.

For the tool to have the greatest impact it should be implemented through a multi-stakeholder process led by the national ministry of health (MOH). This will ensure that all relevant partners understand the associated cost for any sites that they support and that the most up-to-date information is used. An iterative review of inputs and results will ensure that there is broad buy-in and the results will be incorporated into budgets by all stakeholders.

Since the tool is likely to be implemented in resource-limited settings there is sensitivity analysis feature build into the 'Summary' tab which will allow the review group to model the financial impact of incorporating different combinations of quality assurance approaches for varying numbers of devices, facilities, quality assurance activities, users, and mentors. This will allow programs facing budget shortfalls to analyze the relative costs of different quality assurance strategies. However, quality assurance experts should be consulted to analyze the relative patient impact of the various strategies.

Experience Implementing the Quality Assurance Budgeting Tool

The tool was developed in response to a request from the Malawi MOH as they were scaling-up access to CD4 testing through the Alere Pima POC devices. The MOH, in collaboration with the HIV National Reference Laboratory (NRL) and CHAI, conducted an analysis of the budgetary impact on the national quality assurance program of implementing quality assurance for new devices, realizing the need to provide additional quality assurance mechanisms for decentralized testing services.