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Innovation in Global Health

Lessons learned from integrating point-of-care testing technologies for early infant diagnosis of HIV into the national laboratory systems of nine Sub-Saharan African Countries

Module Two

Site and Product Selection; Site Capacity Assessments and Upgrades; and National Approval of Products


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Inputs needed to achieve improved EID outcomes

Key Input Areas

- **Module 1: Leadership, governance, planning and monitoring**
- **Module 2: Site and product selection, site capacity assessments, product approval**
- **Module 3: Site enrollment, orientation, training and competency assessments**
- **Module 4: Site monitoring, support and post-market surveillance**
- **Module 5: Quantification, forecasting, procurement, supply chain and waste management**

Module 6: Quality assurance, data, and connectivity

Observed Outcomes

Compared to centralized, laboratory-based testing, POC EID:

- Increased access to EID test results for HIV-exposed infants;
- Reduced the turnaround time from blood sample collection to return of results to caregivers;
- Increased proportion of test results returned to caregivers;
- Improved timely initiation of ART for HIV-positive infants; and
- Reduced infant morbidity and mortality.

Introduction

This module focuses on **input area two,** site and product selection, which consists of four sub-inputs: (1) site selection; (2) product selection; (3) site capacity assessments and upgrades; and (4) national approval of POC EID products. For each sub-input, the module lists goals, activities, people or organizations involved and resources needed to achieve critical EID outcomes. It also summarize key lessons learned in terms of what worked well, and what did not work well. Finally, the module will provide recommendations and a list of guidance documents, tools, and references that can be used to introduce or scale up POC EID in a country.

Module Two Contents

1. Site Selection for Point-of-Care Early Infant Diagnosis

1.1 Goals

What were the goals of site selection?
Across the nine project countries, the primary goals of site selection were to:

- Increase the number of health facilities with the ability to provide timely and accurate early infant diagnosis and rapid initiation of treatment for HIV-infected infants in accordance with World Health Organization recommendations (see Box 1), while considering current lab functioning;
- Ensure enough testing volume to maintain the proficiency of POC EID instrument operators and ensure a minimum return on investment in POC EID infrastructure by selecting health care facilities, or local networks of facilities, to house POC EID platforms with an average demand of at least 3 tests per work week;
- Optimize previous investments by international donors and development partners in point-of-care technologies by encouraging the uptake of integrated TB and EID testing on existing Cepheid GeneXpert instruments where relevant and available;
- Ensure that sites have adequate capacity for POC EID operations, with a special focus on infrastructure, human resources and waste management capacity
- Select sites that have, or are appropriately linked to, reliable pediatric HIV treatment services.

1.2 Activities and practices

What activities and practices were needed for successful site selection?
The following activities and practices, completed by the ministries of health (MOH) and key stakeholders, were reported as key for reaching the site selection goals:

- Agreement among relevant MOH units and key stakeholders on site selection criteria;
- Mapping existing EID and sample transportation networks;
- Reviewing MOH data and reports, including data dashboards such as district health information systems (DHIS), to determine:

Box 1: WHO Recommendations for Early Infant Diagnosis and Treatment

- All HIV-exposed infants should have a ***virological test at four to six weeks of age*** or at the earliest opportunity thereafter (strong recommendation)[1]
- The turnaround time (TAT) from specimen collection to results return to caregiver ***should never be longer than four weeks.*** (strong recommendation)[2]
- Positive test results should be fast-tracked to the mother-baby pair as soon as possible to enable ***prompt initiation of ART,*** if needed (strong recommendation)[1]
- ***Point-of-care early infant diagnosis of HIV (POC EID)*** can be used for early infant HIV testing (conditional recommendation)[2]
- POC EID testing ***can be used to confirm positive*** test results[3]
- Consideration can now be given to ***replacing RDT at nine months with NAT*** (e.g. POC EID)[3]

[1] World Health Organization (2016). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Second edition. Geneva.

[2] World Health Organization (2010). WHO recommendations on the diagnosis of HIV infection in infants and children. Geneva.

[3] World Health Organization (2018). Technical report. HIV diagnosis and ARV use in HIV-exposed infants: A programmatic update. Geneva.

- The existing EID network, including the number of sites offering PMTCT services in the country, with an emphasis on the geographical distribution and level of infrastructure and services;
- Historic EID testing demand, positivity rates, and proportion of patients receiving their EID results for each site;
- Turnaround time (TAT) from testing to results return for conventional EID; and
- Utilization rates on Cepheid GeneXpert platforms for TB testing.

- Conducting capacity assessments of potential POC EID sites in order to identify gaps in services and assess site-level infrastructure and human resource capacity.[1]
- Creating a preliminary placement plan or roadmap for POC EID.

1.3 Key implementers and collaborators

Who were the key implementers and collaborators?
To implement the above activities, program managers held periodic meetings with MOH representatives and implementing partners, in most cases via national technical working groups (TWG), and made visits to potential POC EID sites to carry out assessments. All countries held discussions and made decisions through some form of TWG to ensure involvement of relevant branches and departments of the Ministry of Health, to coordinate among different organizations and to ensure the availability of reliable information and technical expertise. The types of TWG that led the process of site selection ranged from existing bodies such as the National AIDS Committee or Program; National Laboratory Services Unit or Taskforce; National Pediatric and/or Prevention of Mother-to-Child HIV Transmission (PMTCT) Technical Working Group; or the Procurement and Supply Management Committee.

TWG for POC EID programs tended to be made up of MOH representatives of the National AIDS Control Program or Council as well as of MOH units, such as the PMTCT Unit, Pediatric HIV Unit, National Institute of Health, National Laboratory Unit/Services, or National Reference Laboratory, Sexual Reproductive Health Unit and National TB Program. Sub-national health authorities, such as Provincial or Regional Health Management Teams and District Health Authorities, were also key players in some programs. In addition to EGPAF, other key development partners also participated in the TWG.

1.4 Resources (human, financial and material)

What resources were needed?
All countries reported that national EID data was needed to support technical discussions and reviews for site selection. More than half of the programs reported using transportation and stipends or per diem to support visits to potential POC EID sites. The tool most cited for successful site selection was the EGPAF document, titled *'Proposed criteria for selection of pilot phase sites'*. Another reference tool used was the WHO Information note, *'Considerations for Adoption and Use of Multidisease Testing Devices in Integrated Laboratory Networks'* (See section 5, Guidance, tools and references).

1.5 Results

What were the results of site selection?
National authorities in all project countries identified at least five sites for the early implementation phase. To further increase access to POC EID, eight of the nine countries introduced a short-haul, hub-and-spoke model in which surrounding facilities (spokes, within one hour of the POC EID facility, by any commonly-used form of transport) sent samples to the POC EID testing facility (hub). After six months of close monitoring and learning through the early implementation phase, additional sites were selected in all countries, except one, for the gradual expansion of POC EID testing.

The main results of site selection activities included:
- Agreement on, and rigorous application of, an unbiased set of site selection criteria in each country (see Box 2);
- Development of an initial placement plan for POC EID; and
- Agreement to introduce POC EID in a phased approach, enrolling a limited number of sites or selected geographic areas, such as single provinces in Mozambique, each quarter.

[1] See the Checklist for Assessing the Capacity of Potential POC EID Pilot Sites adapted from the Stepwise Process for Improving the Quality of HIV-Related Point-of-Care Testing (SPI-POCT) Checklist: SPI-POCT Checklist (Instrument based), Version 2.0, 9/16/2014

1.6 Lessons learned

What worked well?

The following were cited as good practices for POC EID site selection:

- Involving all relevant stakeholders and allowing ample time for the MOH and/or TWG to build consensus on POC EID site selection criteria and to develop a POC EID placement plan.
- Placing POC EID instruments in locations within health facilities that allow for the processing of samples from several different entry points (e.g. PMTCT services, nutrition units, pediatric wards) where positivity rates can be much higher than testing through PMTCT services.[2]
- Developing short-haul, hub-and-spoke networks of health facilities to increase access to POC EID for facilities with testing demand of less than three MOH tests per week (see Box 3).
- Consideration of key characteristics of available POC EID products that could limit their ability to be placed in some types of health facilities. For example, some POC cartridges must be incinerated at high temperatures after use. Therefore, it is not possible to install those platforms where there is no access to an appropriate incinerator. In addition, some POC platforms require a stable power supply. Sites with an unreliable power supply require products that include batteries to provide a back-up supply of electricity.
- Final selection should be based on the results of site-level capacity assessments (see Section 3)

Box 2: Site Selection Criteria

The core criteria for POC EID site selection used across the majority of countries were:

- Historical EID testing demand of at least 3 tests per week;
- Historical TAT from sample collection to results received by caregiver of 30 days or more;
- High likelihood for HIV-positive case findings (e.g. historically high positivity rates documented in PMTCT and maternal and child health clinics);
- Located in a priority district, province or region for EID testing;
- Reliable pediatric HIV treatment services available at the site or at a referral treatment site within a reasonable distance;
- Sufficient capacity or level of readiness for POC EID implementation (as measured through a site assessment tool described later in this module);
- If a spoke site, sample transport and regular communication of test results are feasible; and
- For the early implementation phase, located where the performance of the site can be closely monitored.

[2] Cohn J et al. Paediatric HIV testing beyond the context of prevention of mother-to-child transmission: a systematic review and meta-analysis. 2016, 3 (10):e473-81 Lancet HIV

What did not work well?
County representatives suggested that POC EID instruments should not only be placed in exclusively child-centered settings where they would likely be underutilized. In many countries, more needs to be done to ensure platforms are optimally used through integrated testing (e.g. testing for both TB and EID or viral load and EID on one platform).

1.7 Conclusions and recommendations

What recommendations can be made for those intending to adopt the documented activities/practices for site selection?
MOH units responsible for diagnostics and pediatric HIV, together with national public health laboratories and relevant national TWG, agreed on and applied an objective set of site selection criteria that aimed to ensure greater access for HIV-exposed infants to timely and accurate EID testing and rapid initiation of treatment for HIV-infected infants in accordance with WHO standards.[3] The site selection criteria focused on identifying health care facilities, or local networks of facilities, that had sufficient demand for EID testing in order to allow POC EID instrument operators to maintain their proficiency as well as ensure a reasonable return on investment for POC EID testing infrastructure. In most cases, health care facilities with access to decentralized, laboratory-based testing that delivered a large proportion of test results within in 30 days of blood sample collection were not selected for POC EID placement. In addition, when eligible health care facilities already had a near-POC instrument onsite or nearby (e.g. Cepheid GeneXpert), consideration was given to optimizing the unused capacity of those instruments in order to conduct integrated testing for more than one disease (i.e. TB and EID).

Box 3: Hub-and-spoke networks

Short-haul hub-and-spoke networks place a platform in a centrally located hub facility with smaller health outposts, called spokes sites, delivering samples for processing to/from the hub-testing site. When designing hub-and-spoke networks, implementers aimed to ensure that:

- Hub sites had the capacity, including human resources, to process samples from several different health care facilities;
- Samples could be transported in EDTA-treated capillary tubes (e.g. Microvette-EDTA) within 24 hours prior to testing if kept at ambient temperature, and within three days if kept and transported between 2 and 8 degrees Celsius;
- Spoke sites were within a distance of 60 minutes by normal mode of transportation (e.g. car, bicycle, bus, taxi), from the hub site;
- Sample transport from spoke to hub sites used or built on an existing sample transport system; or it was possible to build and sustain a small sample transport system;
- Regular communication between the spoke and hub sites was possible (e.g. by telephone).

In some cases, platforms at hub sites automatically delivered results to an SMS printer at spoke sites. In some countries, such as Lesotho, up to 20% of spoke sites were located more than an hour by typical transport from the hub testing site. In certain cases, rather than selecting a district hospital as the hub testing site, a health center close or on the way to the district hospital was selected instead in order to leverage the existing sample transport system.

[3] (a) World Health Organization (2016). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Second edition. Geneva; (b) World Health Organization (2010). WHO recommendations on the diagnosis of HIV infection in infants and children. Geneva; and (c) World Health Organization (2018). Technical report. HIV diagnosis and ARV use in HIV-exposed infants: A programmatic update. Geneva.

2. Product Selection for Point-of-Care Early Infant Diagnosis

2.1 Goals

What were the goals of product selection?
Across the nine project countries, POC EID product selection aimed to:

- Select technologies that respond to the specific needs and capacity of facilities identified for POC EID testing;
- Ensure that the products selected meet country standards; and
- Ensure the products meet the needs of clients.

For information on securing national approval of POC EID products and assessing the capacity of sites, see Section 3 on Capacity assessments and upgrades and Section 4 on National Approval of Point-of-Care EID Products.

2.2 Activities and practices

What activities and practices were needed for successful product selection?
In the majority of project countries, a side-by-side analysis of products was completed to determine which product was best suited for each of the selected sites. The side-by-side analysis included the following considerations:

- Instrument throughput capacity (i.e. the number of tests that can be run per day on an instrument);
- The amount of time required to process a single test (i.e. time to result);
- Testing cartridge shelf life;
- Temperature and electricity requirements;
- Availability of backup power (i.e. testing instrument has a built-in battery);
- Routine maintenance needs;
- Instrument portability and polyvalence (i.e. ability to perform more than one type of test);
- Connectivity function (i.e. ability to transmit data from the instrument over the internet) for remote management and results transmission, including the ease of implementation and associated costs of the connectivity solution;
- Type of sample needed (e.g. whole blood);
- Requirements for the safe disposal of test cartridges;
- The price of the platform, testing cartridges, extended warranty, connectivity, consumables and accessories (e.g. computer, modem, printer, external battery system); and
- The type of HIV detected by the instrument (e.g. HIV1, HIV2).

Other considerations included:

- The existence of stringent regulatory approval of available products;
- The need for in-country registration of available products;
- Availability of a stable supply of electricity and access to high temperature incineration facilities at the selected sites;
- Sample preparation needs;
- Calibration and maintenance needs of the instrument;
- Shipping and storage requirements (e.g. packaging size, temperature, secured rooms, etc.); and
- Terms, conditions, and coverage of service and maintenance agreements.

2.3 Key implementers and collaborators

Who were the key implementers and collaborators?
In most project countries, the MOH laboratory units played a key role in product selection; and in many cases, alongside the National AIDS Control Authority. Most countries also held discussions and made decisions through some form of TWG that included the MOH AIDS and Sexually Transmitted Infection (STI) Control Program, TB, PMTCT and Sexual and Reproductive Health Units, Prevention Unit as well as bodies such as the National Public Health Reference Laboratory and partners such as EGPAF, URC, USAID, CDC, CHAI and UNICEF.

2.4 Resources (human, financial, and material)

What resources were needed?
Overall, representatives in the project countries reported that there were adequate tools and resources to support product selection. Resources found to be helpful, and provided by the MOH in some countries, included stipends to support field visits related to product selection, as well as the hosting of meetings to discuss and review product selection. There was unanimous use of the *WHO pre-qualified products list as well as the EGPAF site and product selection approach document and the EGPAF side-by-side analysis* of products document. Several countries relied on the WHO information note titled *Considerations for adoption and use of multidisease testing devices in integrated laboratory network*s (2017), as well as documentation on the platform fabrication process.

2.5 Results

What were the results?
During the first round of product selection in 2016, three POC EID products had recently entered the market, with only two having received WHO prequalification. Given the limited number of WHO pre-qualified products to choose from, the selection process focused on the following site-level characteristics: (a) the daily testing demand at each site; (b) the availability of a reliable source of electricity; (c) access to a high-temperature incinerator for the disposal of testing cartridges; and (d) type of HIV detected.

The Alere Q product, now called the Abbott m-PIMA, was selected for sites with a demand of less than eight tests per day, and/or an unstable electricity supply, and/or lack of access to a high-temperature incinerator. This is because of its single module that can process a maximum of eight tests per day, its built-in battery, and its use of cartridges that do not require special incineration. The Cepheid GeneXpert product was frequently selected for larger, more centralized facilities with greater human resource capacity, higher testing volumes, a stable supply of electricity, or the possibility to install an alternative power backup system, and access to a high-temperature incinerator. The Cepheid GeneXpert instrument has four modules that can process up to 20 tests per day, but does not come with a built-in battery and uses cartridges that require high-temperature incineration. For sites with existing Cepheid GeneXpert instruments, where agreements were reached for integrated TB and EID testing, special efforts were made to gain access to high-temperature incinerators and, if needed, to install a backup electricity system.

In four of the nine project countries, both the Abbot m-PIMA and the Cepheid GeneXpert products were selected for different types of sites in order to gain experience with both products, benefit from comparison, and inform future scale-up of POC EID. In the remaining five project countries, the Abbot m-PIMA product was the only product selected for all POC EID sites.

2.6 Lessons learned

What worked really well?
Across all project countries, relevant stakeholders were involved in all stages of product selection, from the side-by-side analysis to final product selection. One country reported that their national laboratory leadership structure facilitated implementation and uptake of new technologies.

Others reported the involvement of POC EID product manufacturers in the process as a good practice, because they were able to respond to questions about the product and become more familiar with the needs of national programs. EGPAF program implementers, decision makers, implementation partners, government officials and staff at health care facilities found collaboration, sharing of information and transparency to be important.

Representatives in at least one country reported that it is important to carry out site selection and product selection simultaneously to ensure the right machines are in the right locations. In another country, it was reported that site and product selection should be performed as an iterative process with site characteristics informing product selection and product characteristics further informing and refining site selection. However, plans changed in that country due to delays in the national approval process for the POC EID products, and as a result, the site selection went ahead first. This highlighted that dynamics may change midway in implementation, and implementers should be flexible and ready to change the product if not yet installed or move it to where it is optimally used.

What did not work well?
Respondents in one country advised to avoid selecting more than one product in the initial phase as it caused a burden on procurement and human resources by needing to manage more than one supplier and to train staff in more than one technologies. It was suggested to minimize these until the lessons-learned are understood and then scale-up the program. However, in another country it was reported that selection of just one product for the pilot phase meant that there was not sufficient exposure or experience with other products when it came time to scale up, which limited the ability to make an informed selection.

Not exploring the possibility of integrated TB and EID testing on a single instrument was seen as a missed opportunity in one country. In addition, the relatively short shelf life of testing cartridges (i.e. 9 to 12 months from manufacture date) was reported to pose a challenge to the further roll out of POC EID. Finally, uncertainties related to the funding and procurement of testing cartridges after the close of the EGPAF project was seen in one country as a challenge to sustained use of the products.

2.7 Conclusions and recommendations

What recommendations can be made for those intending to adopt the documented activities/practices?
In most project countries, the MOH laboratory units led the selection of POC EID products in consultation with other key stakeholders, such as the National AIDS Control Authority. Product selection was based on an objective and transparent analysis of information about available, WHO-prequalified products and the sites where they would be placed. This approach allowed for the application of the fit-for-purpose principle, whereby product characteristics were analysed with respect to the infrastructure, human resource capacity, and needs of the proposed testing sites.
Important site-level characteristics that were considered during product selection included:

- The availability of appropriate infrastructure and human resources, including a stable supply of electricity;
- Environmental conditions of the proposed testing location, including temperature, cleanliness, and amount of space;
- Estimated testing volumes to ensure that the product will be neither under-utilized nor lack the capacity to meet the testing demand;
- Access to appropriate waste disposal facilities for used testing cartridges;
- The need for integrated testing on a single POC instrument, such as integrated TB, EID and viral load testing; and
- Possible need for a POC technology that can be used in a mobile unit or moved between testing sites.

3. Site Capacity Assessments and Upgrades

3.1 Goals

What were the goals of site capacity assessments and upgrades?
In all project countries, the goals of site capacity assessments and upgrades were

- Determine if a healthcare facility met minimum standards for POC EID testing;
- Identify where to place a POC instrument within the site; and
- Identify and implement site upgrades, as needed.

3.2 Activities and practices

What activities and practices were needed for successful site capacity assessments and upgrades?
In all project countries:

- A preliminary list of POC EID sites was developed.
- An MOG unit sent an official communication to alert sites of the capacity assessments and to demonstrate ownership of the initiative by MOH.
- Capacity assessments were conducted using a standardized assessment tool adapted from the *Stepwise process for improving the quality of HIV-related point-of-care testing (SPI-POCT)* tool developed by CDC.
- Based on the results of the assessment, each health facility received a score indicating its level of readiness for POC EID introduction and a tentative improvement plan was drafted to ensure that the site met minimum standards for POC EID should it be selected for implementation.
- The results of site capacity assessments were presented and discussed with the MOH and/or relevant TWG and a decision was made about which sites should be taken forward for POC EID introduction.
- Where needed, upgrades were completed at sites that were selected for POC EID and that required them as part of their site improvement plan.

3.3 Key implementers and collaborators

Who were the key implementers and collaborators?
In most project countries, the MOH laboratory units played a key role in site capacity assessments with contributions from the relevant national TWG. The TWG typically included representatives of the MOH PMTCT and Pediatric HIV Units as well as the National AIDS Authority or Committee. Sub-national MOH representatives such as district health authorities, and partners such as EGPAF, CHAI and UNICEF were also involved in site capacity assessments.

3.4 Resources (human, financial, and material)

What resources were needed?
Depending on the country, one to five people were needed to carry out each site assessment, most of whom were project staff requiring some financial resources such as per diem for food, lodging, and transport. The primary tool used to carry out the assessments was the 2017 version of the *EGPAF checklist for assessing the capacity of potential POC EID testing sites,* which was adapted from the Stepwise Process for Improving the Quality of HIV-Related Point of Care Testing (SPI-POCT) Checklist, developed by the U.S. Centers for Disease Control and Prevention (CDC). The SPI-POCT checklist was designed for any instrument-based POC device (e.g. early infant diagnosis, CD4, viral load).

3.5 Results

What were the results?
In most countries, capacity assessments were conducted at all potential sites prior to approving a site for POC EID introduction. In other countries, only a sub-set of healthcare facilities were assessed. The assessments helped determine which sites were best suited for POC EID placement as well as the types of improvements or upgrades needed to prepare each site. The assessments also helped inform decisions about which type of POC EID product was best suited for the site.

For health care facilities that required improvements or upgrades, a site improvement plan was developed. Common types of upgrades needed included:

- Reinforcement of windows and doors for rooms where the POC platform was located;
- Locks for windows, doors and/or cupboards;
- Tables for POC platforms;
- Shelves or cabinets to store POC commodities (e.g. sample collection kits, testing cartridges);
- Thermometers for rooms where the platform was located;
- Installation or repair of electricity and/or plumbing;
- Installation of air conditioners for rooms where the platform was located;
- Installation of batteries and/or power inverters for Cepheid GeneXpert platforms; and
- Surge protectors and power adaptors with electrical extension cables.

Additionally, in countries that applied the short-haul, hub-and-spoke network model there was a need for cooler boxes and bags for sample storage and transport. At least two countries used motorcycle riders (either contracted our employed by the MOH) for sample transport.

The assessments helped develop a more complete picture of the program. In addition to assessing the level of readiness for POC EID introduction, the results also revealed information on:

- Tools and the integration of HIV/TB;
- Training and competency;
- Physical infrastructure;
- Supplies, reagents and equipment;
- Testing procedures and M&E/QA; and
- Level of acceptance of initiative by facility staff

3.6 Lessons learned

What worked really well?
The following were reported as good practices for site capacity assessments and upgrades:

- All potential sites should be assessed before making a final decision about where to place POC instruments.
- The results of site capacity assessments can be used to make a final decision about whether or not to enroll each site and to identify the improvements or upgrades needed to fully prepare a site for POC EID testing.
- If a site does not meet required standards, the site improvement or upgrade plan can be implemented in order to ensure that the site qualifies for POC EID placement.
- The assessments, overall, served to identify gaps in the preliminary site selection plan that could be learned from and acted on; determine if integrated HIV/TB testing was possible at a site; inform decisions about the best type of POC EID product to place at each site; and increase the involvement of health facility staff.

During the capacity assessments, the patient flow and facility work flow for each site were considered in order to understand where to place the POC EID platform. This was important to ensure that all service delivery entry points were captured in order not to miss children who are eligible to be tested. Some of the facilities were collecting samples on different days from when the courier ('health rider') visited to collect samples, so arrangements were made for a change in patient flow and the days of drawing blood were changed.

One good practice observed was a brief project orientation with the facility, district, and provincial leadership for early buy-in in case the site was formally selected. One key informant reported that site capacity assessments allowed the MOH to take the lead in the final selection of sites, based on MOH priorities for EID.

One country held two assessments, each one year apart, and found that, in some cases, the placement of the platform had changed and the consultation room or machine was now in a different location (at the same facility) than before, not necessarily better or worse location, but this change needed to be recorded. If site assessment had been carried more than a year before, it was worth performing a rapid assessments of key issues to determine if the site was still ready.

What did not work well?
Some site upgrades were not completed prior to the installation of the POC platform and initiation of testing services due to delays encountered whilst working with relevant government departments responsible for facility upgrades, which was identified as a challenge to introducing POC EID testing.

In order to avoid misconceptions, one key informant highlighted the importance of explaining to health care facility staff that the POC platform can be placed in the clinic with the nurse or other health care workers. For example, health care workers, such as nurses, can use the platform to run the test in the consultation room. It is not necessary to upgrade the health care facility infrastructure by building a lab. This was not initially clear in one of the project countries.

Finally, one country reported room for improvement in terms of staff responsibilities and the analysis of human resource capacity. The presence of POC EID adds new responsibilities to clinical personnel who may feel like additional duties are being assigned to them, for which they are not receiving additional compensation. The capacity assessments should include a general analysis of staff workload and the reductions and/or additions to workload that would be created by POC testing. At the minimum, it would be important to update the job descriptions of clinical staff in order to include responsibility for processing point-of-care tests.

3.7 Conclusions and recommendations

What recommendations can be made for those intending to adopt the documented activities/practices?

Site capacity assessments should be used to help determine:

- If a site is ready to implement POC EID;
- If any improvements or upgrades are needed at a site prior to introducing POC testing; and
- What type of POC products are best suited to the particular characteristics of the site.

In addition, site assessments should involve an analysis of the human resources available to conduct POC testing, including the current and predicted future workload of those staff. And the assessment should analyze patient flow and work flow in order to inform where and how to integrate POC testing into current service delivery practices.

It is important to carefully consider where the POC platform should be located within a health facility in order to provide the greatest access to POC EID testing for both PMTCT services as well as non-PMTCT services (e.g. nutrition unit, pediatric wards). Futhermore, it is not necessary to place the platform in a lab or to build a lab onsite for the platform. The platform can be placed in any secure location within the health facility.

The capacity assessment can also serve as an opportunity to orient staff and engage them early in the process of introducing POC testing.

[4] World Health Organization (2003). Aide-Memoire on Strengthening National Regulatory Authorities. (https://www.who.int/medical_devices/publications/aide-memoire-strengthening-national-regulatory-authorities/en/)

4. National Approval of Point-of-Care Early Infant Diagnosis Products

4.1 Goals

What were the goals of national approval of POC EID products?
Medical technologies, and specifically diagnostic instruments and testing cartridges, should be approved by or registered with a national regulatory authority (NRA) before they can be procured and routinely used for patient management. The role of the NRA is to ensure that valuable new technologies are made available to the clinical community and to patients and consumers as quickly as possible while preventing unsafe and ineffective devices from reaching the market.

In the project countries, the primary goals of national product approval were to:

- Verify that POC EID products were of assured quality, safety and efficacy;
- Ensure that new medical products were accompanied by appropriate information to promote their rational use[4]; and
- Verify test performance characteristics as outlined by the manufacturer.

4.2 Activities and practices

What activities and practices were needed for successful national approval of POC EID products?
In all project countries, activities focused on ensuring that POC EID products, both platforms and testing cartridges, were registered and/or approved by the appropriate NRA before procuring and importing them into a country for routine clinical use.

In some countries the approval process was well described, publicly available, and followed a single, unified approach for all products, but in most countries it was not. All project countries required WHO prequalification of POC EID products before they could be considered for national approval. One country had no additional requirements beyond WHO prequalification, while one country (Eswatini) required a short laboratory validation and verification of the Alere Q platform, which compared the test performance of Alere q NAT POC-EID technology, detecting HIV-specific RNA in whole blood samples, with that of a conventional laboratory-based method for EID (Roche Cobas AmpliPrep /Cobas TaqMan (CAP/CTM) HIV-1 qualitative assay) conducted on DBS samples. Results showed that Alere q HIV 1/2 Detect showed exceptional overall concordance with the standard of care (SOC) assay, with an overall high sensitivity of 96.4% and specificity of 100% respectively. These findings were concordant with performance characteristics as established by the manufacturer. Three other countries required both a lab validation or verification as well as a pilot study or field evaluation. The field evaluations involved analyzing hundreds of blood samples on the POC EID platform and sending samples from the same patients for analysis on laboratory-based instruments in an effort to demonstrate a concordance between the two approaches. These evaluations took anywhere from three to six months to complete and required the development and use of rigorous study protocols that were reviewed and approved by local ethics committees or internal review boards (IRBs). In one country, three distinct steps were needed to obtain full approval: a validation of products by an independent lab in order to obtain approval from the medical laboratory board; registration of the products with the poisons and medicines board; and presentation of the products to the MOH equipment committee in order to add them to approved products list. In another country, the results from field evaluations conducted in other countries were considered in the approval process. Finally, due to the absence of a formal NRA or registration process in two countries, EGPAF obtained a waiver from the Permanent Secretary of the National AIDS Control Program to import and use POC EID products in those countries.

At an international level, a group called the EID consortium completed nine independent field evaluations of Alere q (now Abbott m-PIMA) and Cepheid GeneXpert platforms and cartridges in six countries (Kenya, Malawi, Mozambique, Tanzania, South Africa and Zimbabwe). The analysis found that both products performed well in the field. The

consortium presented their findings at the July 2016 AIDS Conference in Durban, South Africa, and at a technical consultation convened by WHO and the African Society for Laboratory Medicine (ASLM) in October 2016, which aimed to help overcome regulatory barriers for POC EID.[5] In 2017, the WHO released an information note titled Novel point-of-care tools for early infant diagnosis of HIV (http://www.who.int/hiv/pub/toolkits/early-infant-diagnosis-hiv-2017/en/), which urged national regulatory agencies to adopt a rapid and streamlined registration and national approval process for immediate implementation of POC EID.

4.3 Key implementers and collaborators

Who were the key implementers and collaborators?
National entities responsible for the approval and/or registration of medical products ranged from independent national boards, such as national laboratory or medicines boards, to the national laboratory unit or committee within the MOH. Where these committees or boards did not exist, the Permanent Secretary of the National AIDS Committee or the MOH stepped in to officially approve the products for routine use in their countries.

The approval process was often supported by relevant MOH departments, such as the AIDS and TB Units, monitoring and evaluation unit, national laboratory unit, directorate of diagnostics and clinical care services, directorate of laboratory services or the sexual and reproductive health unit. The National AIDS Program or Committee and relevant TWG and implementing partners, such as EGPAF, CHAI and UNICEF also supported the national approval efforts. In half the project countries, POC EID product manufacturers themselves were involved in the approval process, primarily donating platforms and testing cartridges to support various verification, validation, and field evaluations.

4.4 Resources (human, financial, and material)

What resources were needed?
Resources for the various verifications, validations and field evaluations required for product approval or registration included:

- IRB-approved study protocols (where a formal field study was required):
- Blood samples;
- Platforms and cartridges donated by the manufacturer or procured by implementing partners;
- Human resources to conduct the studies and evaluations;
- Validation and verification reporting tools, data analysis tools, results reporting tools and written reports.

In two countries, the national approval took less than six months. In all other countries, the process extended well beyond six months.

4.5 Results

What were the results?
In the majority of project countries, a certificate or letter was issued confirming approval and authorizing routine use of products. In two countries, a project-specific waiver for routine use was given while a process of national approval was being defined. In all countries which received clearance, the certificate was also returned to the manufacturer. In half the countries, an assessment was performed to identify how the process of national approval could be streamlined for future products.

4.6 Lessons learned

What worked really well?
Including a representative from the approval body in the POC EID program's TWG was reported as a good practice as updates on product approval could be given in real time. In those countries which had involvement from the machine manufacturer, that involvement was information sharing by the in-country manufacturer's representative, this was seen as good practice.

Where a laboratory technical working group met as part of the approval process, one good practice identified was that partners in the group provided evidence to inform the approval of POC EID.

One country does not have a regulatory body for lab products, it relies on WHO qualification status. The program team verified that the products were WHO pre-qualified, then identified the products needed using a SWOT analysis. This was followed-up with a validation and verification of products which resulted in program staff having confidence in the products.

[5] AIDS 2016. Field performance of point-of-care HIV testing for early infant diagnosis: pooled analysis from six countries from the EID Consortium. Poster presentation (http://programme.aids2016.org/Abstract/Abstract/10602 and https://eidconsortium.org/Files/EID%20Poster%20v5%20Low%20res.pdf).

What did not work well?
Key informants in several project countries reported that laboratory validations and field evaluations required by national regulatory bodies produced limited added value when WHO prequalification was in place. Additionally, the pooled results of the EID consortium evaluations across six countries, consumed scarce resources that could have been used for diagnosing and treating HIV-positive infants.

In two countries, it was difficult to identify the national regulatory body, or bodies responsible for approval of diagnostic products did not exist. In two other countries conditional approval was given in certain sites, or for studies, but the product was not fully approved. In one country, registration requirements were cumbersome and lengthy. In another country, an implementing partner was responsible for laboratory and field evaluations on behalf of the MOH, which led to delays in EGPAF program implementation.

4.7 Conclusions and recommendations

What recommendations can be made for those intending to adopt the documented activities/practices?

National regulatory authorities, where they exist, have different requirements, but also have shown increasing commitment to leveraging existing data and work already performed. According to WHO, sufficient evidence has been generated on the performance of the Alere Q (now Abbott m-PIMA) and the Cepheid GeneXpert POC EID assays in the intended field settings to support rapid national regulatory approval and initiation of scale-up. Performance was consistent between laboratory and field settings, and across countries. Further technical evaluations of these technologies are unlikely to add value, but may instead delay implementation and timely diagnoses of HIV-infected infants, a critical and vulnerable population. National regulatory agencies are, therefore, encouraged to not delay adoption by conducting further evaluations, but instead adopt a rapid and streamlined registration and national approval process for immediate implementation. To support this effort for both POC EID and future diagnostic products, WHO committed, in December 2018, as part of the high-level dialogue to assess progress on and intensify commitment to scaling up diagnosis and treatment of pediatric HIV, to develop and implement a sustainable and affordable collaborative registration procedure for diagnostics and support national regulatory bodies to make use of it to streamline their national regulatory procedures.

5. Guidance, Tools, and References

Several of the following guidance, tools and references are available through the ASLM/CHAI/EGPAF/CDC/WHO/UNICEF/Unitaid, **HIV Point-of-Care Diagnostics Toolkit**. Available at: http://childrenandaids.org/poc-site-product

5.1 Guidance documents

The following documents provide guidance for how complete site and product selection and site capacity assessments and upgrades.

1. EGPAF/Unitaid, (November 2018). **POC EID site and product selection approach.** https://www.pedaids.org/wp-content/uploads/2020/02/01_Site-and-Product-Selection-Approach_EGPAF_FINAL_10Nov2018.docx

2. EGPAF/Unitaid, (November 2018) **Guidance for supporting national ministries of health and technical working groups to develop or update an operational strategy or plan for scaling-up access to POC EID within an integrated laboratory network.** https://www.pedaids.org/wp-content/uploads/2020/02/02_Guidance_EID-Network-Plan_FINAL_10Nov2018.docx

3. EGPAF/Unitaid, (December 2017). Guidance note on product selection, facility upgrades and sample transportation. Available at POC toolkit page (http://childrenandaids.org/node/981).

4. EGPAF/Unitaid, (August 2016). **Proposed criteria for the selection of pilot phase sites.** https://www.pedaids.org/wp-content/uploads/2020/02/04_Criteria_Site-Selection_Pilot-Phase_EGPAF-POC-EID_Aug2016.docx

5. World Health Organization (2015). **Post-market surveillance of in vitro diagnostics.** Available at: http://apps.who.int/medicinedocs/en/m/abstract/Js23511en/

5.2 Tools

The following tools will support implementers in completing site and product selection and site capacity assessments and upgrades.

6. EGPAF, (June 2018). **Side-by-Side Analysis of POC EID Products.** Previous, 2017 version, available at POC toolkit page (http://childrenandaids.org/node/982). https://www.pedaids.org/wp-content/uploads/2020/02/06_Side-by-Side-Analysis_POC-EID-Products_27June2018.docx

7. EGPAF/Unitaid, (February 2017). **Checklist for assessing the capacity of potential POC EID testing sites (adapted from the SPI-POCT).** https://www.pedaids.org/wp-content/uploads/2020/02/07_Adapted_SPI-POCT-Capacity-Assessment_UPDATED_10Feb2017.docx

8. ASLM. **Planwise** – Geospatial Planning Tool. Available at: http://www.aslm.org/what-we-do/laboratory-mapping/

9. USAID. **Laboratory Efficiency and Quality Improvement Planning tool (LabEQIP).** Available at: https://www.ghsupplychain.org/resource/labeqip

10. CHAI. **Integrated EID-VL Product and Site Selection Analysis Tool.** Available at POC toolkit page: (http://childrenandaids.org/node/980)

11. The Global Fund, (2017). **HIV viral load and early infant diagnosis selection and procurement information tool.** (https://www.theglobalfund.org/media/5765/psm_viralloadearlyinfantdiagnosis_content_en.pdf)

12. LSHTM, (2014). **Generic Protocol for POC EID Test Evaluation.** Available at POC toolkit page: (https://idc-dx.org/resource/generic-protocol-for-poc-eid-test-evaluation-2014/)

5.3 References

The following references provide key information to support site and product selection, site capacity assessments and upgrades, and national registration of POC EID products.

Alemnji G et al., (2017). **Improving laboratory efficiencies to scale-up HIV viral load testing,** Current Opinion in HIV and AIDS. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28059956

Carmona S et al. (2016). **Field performance of point-of-care HIV testing for early infant diagnosis: pooled analysis from six countries from the EID Consortium.** AIDS 2016. Poster presentation (http://programme.aids2016.org/Abstract/Abstract/10602 and https://eidconsortium.org/Files/EID%20Poster%20v5%20Low%20res.pdf).

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International Organization for Standardization, (2016). **ISO Point-of-care testing (POCT) – Requirements for quality and competence.** Available at: https://www.iso.org/obp/ui/#iso:std:iso:22870:ed-2:v1:en

LSHTM (2014). **Summary of regulatory oversight of in-vitro diagnostics in selected African countries.** Available at: http://www.idc-dx.org/resources/summary-of-regulatory-oversight-of-in-vitro-diagnostics-in-selected-african-countries

McNerney R et al. (2014). **Improving access to new diagnostics through harmonised regulation: priorities for action.** African Journal of Laboratory Medicine. Available at: https://ajlmonline.org/index.php/ajlm/article/view/123

World Health Organization (2018). **Technical report. HIV diagnosis and ARV use in HIV-exposed infants: A programmatic update.** Geneva. Available at: https://www.who.int/hiv/pub/paediatric/diagnosis-arv-infants/en/

World Health Organization, (2017). **Considerations for Adoption and Use of Multidisease Testing Devices in Integrated Laboratory Networks**, Geneva. Available at: http://who.int/tb/publications/2017/considerations_multidisease_testing_devices_2017/en/

World Health Organization (2017). **Novel point-of-care tools for early infant diagnosis of HIV**, Geneva. Available at: http://www.who.int/hiv/pub/toolkits/early-infant-diagnosis-hiv-2017/en/

World Health Organization (2016). **Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Second edition.** Geneva. Available at: https://www.who.int/hiv/pub/arv/arv-2016/en/

World Health Organization (2010). **WHO recommendations on the diagnosis of HIV infection in infants and children.** Geneva. Available at: https://www.who.int/hiv/pub/paediatric/diagnosis/en/

World Health Organization. **Technical guidance series for WHO prequalification of IVDs,** WHO. Available at: http://www.who.int/diagnostics_laboratory/evaluations/en/

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