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 Four

Site Monitoring, Support, and Post-Market Surveillance

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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 four,** which includes two sub-inputs: (1) site monitoring and support for POC EID; and (2) post-market surveillance. For each sub-input, the module lists goals, activities, people, or organizations involved, as well as resources needed to achieve WHO-recommended EID outcomes. It also summarizes lessons-learned in terms of what worked well, and what did not work well. Finally, the module provides 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 Four Contents

1. Site Monitoring and Support for Point-of-Care Early Infant Diagnosis

1.1 Goals

What were the goals of site monitoring and support?
Regular monitoring of POC EID implementation is crucial to ensure that healthcare services consistently deliver valid and reliable test results. Monitoring visits provide essential insights into key elements of POC EID testing, such as human resources, patient flow, platform functioning, instrument operator performance, specimen transport, record keeping, and capacity building needs of site-level staff. Through site visits, supervisors can identify small issues early, and work with the healthcare facility staff to address them before they become large problems. Site visits also can be used to build the capacity of healthcare providers and POC EID platform operators.

1.2 Activities and practices

What activities and practices were needed for successful site monitoring and support?
Site monitoring visits were carried out soon after the enrollment of all POC EID testing sites, at two weeks, six weeks, and 12 weeks after enrollment, and then subsequently at quarterly intervals. The timing of each visit was communicated in advance to the healthcare facility. Ad hoc site monitoring visits were also made when a problem was identified that required immediate action.

During site monitoring visits, the following aspects of POC EID testing were observed and evaluated:
- clinical Integration, comprising a review of patient registers and patient flow;
- presence and quality of standard operating procedures (SOPs), job aids, and other relevant documentation;
- instrument operator training and performance;
- instrument placement and performance;
- inventory and waste management; and
- linkage of patients to treatment and care.

Monitoring visits assessed how well testing algorithms were being followed and checked the accuracy and completeness of a number of POC EID processes, including, for example, the quality and accuracy of filling in testing forms; drawing blood samples; processing POC EID tests; labeling, packaging, recording and transporting blood samples from spoke to hub sites; communicating test results to caregivers; managing POC EID supplies; and disposing of POC EID waste.

Site support was provided in response to issues identified during site monitoring visits and in response to specific requests from heads of health facilities.

Common site support activities included:
- mentoring, training, and information sharing with healthcare facility staff;
- process-related adjustments;
- printing and distribution of tools such as job aids;
- procurement of items such as those listed below under 'resources';
- improvements to site infrastructure;
- improvements in waste management (e.g. provision of color-coded bins, biohazard bags);
- working with MOH to implement mentoring or refresher trainings;
- support to coordination meetings; and
- improvements to patient tracking mechanisms.

1.3 Key implementers and collaborators

Who were the key implementers and collaborators?
In all project countries, site monitoring visits were planned and implemented with sub-national MOH staff (e.g. provincial, regional district, county) with the support of national MOH units (in conjunction with other laboratory monitoring activities). Collaborators included the MOH, the National AIDS Control Committee, and implementing partners, such as EGPAF.

1.4 Resources (human, financial and material)

What resources were needed?
MOH staff received training to conduct site monitoring visits and typically conducted them together with implementing partners, such as EGPAF. Each member of the site monitoring team required travel and subsistence allowances to conduct the visits.

Site monitors used the <u>Guidance Note on POC EID Site Monitoring</u>, which includes a recommended schedule for conducting site monitoring visits and suggestions for factoring human resource capacity into the scheduling of site monitoring visits.

In addition, the following supporting checklist were used:
• Site Monitoring Checklist: Stand Alone Testing Site
• Site Monitoring Checklist: Hub Testing Site
• Site Monitoring Checklist: Spoke Site

Financial resources were needed for training, accommodation for site monitoring staff, transportation fees, per diem, and airtime to communicate with healthcare workers at POC EID sites.

To overcome challenges identified in the site monitoring, additional materials were provided to a number of health facilities depending on the identified needs. Not all health facilities required additional resources. Examples of additional materials includes:
• printed algorithms, job aids, logbooks, and POC EID testing forms;
• room and fridge thermometers;
• scanners for testing sites;
• computers to support data entry;
• cooler boxes and sample transport kits at spoke sites to support blood sample transport;
• air conditioners and/or power inverters for some cepheid sites;
• reinforcements and/or locks for windows and doors;
• lab chairs, tables for POC instruments, and shelves to store POC commodities;
• support for waste management; and
• upgrades to electricity and plumbing for spaces allocated to POC EID service provision.

Where site monitoring revealed issues with the transmission of test results from testing sites to spoke sites, EGPAF supported the installation of SMS printers and/or the provision of airtime to improve communications between hubs and spoke sites.

1.5 Results

What were the results of site monitoring and support?
Common challenges identified during site monitoring visits included issues related to analyzing and

responding to instrument internal quality control (IQC) failures; incomplete or inaccurate POC EID testing forms; poor clinic staff knowledge of the EID testing algorithm; turnover and/or inappropriate training of clinic staff; inadequate systems for stock and waste management; poor coordination among testing entry points; and poor sample transport and communication between hub and spoke sites. Initial monitoring visits found that many testing sites had poor security, lack of room-temperature monitoring, and lack of storage capacity for POC commodities. Some visits found delays in processing samples transported from spoke sites to hub testing sites.

Challenges were overcome through improvement plans developed during the monitoring visits. For example, where operator-related IQC failures were reported, training and mentoring were conducted to reduce those failures. Initially, site monitoring identified a greater quantity and frequency of IQC failures, but with site support and training, IQC failures decreased. For example, some IQC failures were related to errors in loading testing cartridges into instruments and the use of powdered gloves, which interfered with the correct functioning of the POC EID instruments. This trend was addressed by mentoring platform operators, procuring of powder-free gloves and a specific job aid on how to close the instrument door. These actions led to a decrease in testing cartridges lost to errors. During site monitoring, one country observed that some blood samples were clotted. A solution was the procurement of cooler boxes, and now, all spoke sites have them. In addition, in several countries, support was given to update testing algorithms, standard operating procedures, and job aids, especially to track IQC failure rates and cartridge consumption. This type of support was found to be highly beneficial.

Key outcomes of site support:
• instrument IQC failures decreased;
• fewer testing cartridges were lost to IQC failures; and
• the turnaround time from sample collection to receipt of test results by caregivers decreased, particularly at spoke sites.

EGPAF facilitated discussions with manufacturers and country-level decision makers on connectivity solutions in order to remotely monitor and support testing sites, and on the use of SMS printers at spoke sites for the rapid relay of test results from hub to spoke sites. In most countries, a connectivity

agreement between the manufacturer and the MOH was made, outlining the roles and responsibilities of each party and defining data ownership and security measures set in place, in order to ensure sustainability.

1.6 Lessons learned

What worked really well?
Conducting site visits together with national, regional or district MOH staff was beneficial to improve understanding of POC EID, ensure MOH ownership of POC EID, and institutionalize the activity.

Site monitoring, combined with remote monitoring of instruments using connectivity solutions worked well, not only for quality assurance, but also as a way to assess testing cartridge consumption and IQC failures and make changes to address those challenges.

Mentoring staff in POC EID sites helped improve testing results. Mentorship incorporated capacity-building and quality improvement elements. For newly enrolled sites, mentorship was directed at building confidence (ex. in filling out the lab request form). The activity was particularly successful when it included discussions with heads of facilities.

What did not work well?
Scheduling of visits was a challenge, particularly in countries that required prior authorization to visit a health facility (e.g. a service note). When authorization was not obtained in time, monitoring visits were delayed, and often had to be re-scheduled. Some countries found that site-monitoring visits did not always coincide with tests being performed. It was not easy to monitor instrument operators, because visits were not always scheduled at the same time that a blood sample was collected or received for testing. Making site visits when there were cases to assess is noted as a challenge.

Additionally, it was found that in order to monitor the testing procedure from sample collection to return of results, it was necessary to stay longer at the site than foreseen, leading to delays in the scheduling of other site monitoring visits.

1.7 Conclusions and recommendations

What recommendations can be made for those intending to adopt the documented activities and practices for site monitoring and support?
As POC EID is a new technology, it is important

to support sites to carry out decentralized services. It is recommended for the MOH to integrate site monitoring into standard site supervision procedures and tools and continue to observe POC EID testing and provide feedback and mentoring as needed. The MOH should plan and implement site monitoring together with relevant implementing partners in order to ensure broader views and perspectives on POC EID activities. Communication with the head of the health facility being monitored is important, as is working in close collaboration with the relevant sub-national hospital and laboratory, to ensure that they are involved in site monitoring activities.

Conduct site monitoring on-site, at the facility being monitored, rather than asking staff to meet in another location. Schedule site monitoring visits on assigned clinic days to allow observation of the whole process from sample collection to return of results. In the event that a site monitoring visit does not coincide with POC EID testing activities, make a return visit so it is possible to observe the instrument operator and machine in use. Connectivity has the potential to make financial savings in terms of number and frequency of site monitoring visits.

Create a healthy competition between sites for improved performance by rewarding best-performing sites (based on some pre-determined indicators) quarterly, semi-annually or annually, whichever is more feasible.

Site monitoring and support visits should be used as an opportunity to remind healthcare facility management of the importance of maximizing the use of the POC EID platform by ensuring that eligible infants from other entry points within the facility, such as pediatric wards and nutrition units, have access to the service.

Boost motivation by making it possible for some mentees to graduate from the mentorship program and become mentors themselves to provide local mentorship, thus reducing the need for external mentorship. Encourage integration of POC EID into the other activities of the visited health facilities by organizing post-mentorship feedback meetings with core staff, so that mentorship does not only benefit the individuals mentored, but also helps to build the capacity of the entire health facility.

2. Post-market Surveillance

2.1 Goals

What were the goals of post-market surveillance?
The goal of post-market surveillance is to protect individual health and public health by ensuring that in vitro diagnostics (IVDs) continue to meet the same quality, safety, and performance requirements they met when they were initially placed on the market. This entails both proactive and reactive surveillance. Proactive post-market surveillance can include lot verification testing, both before and after distributing test kits to sites. Reactive post-market surveillance involves reporting and evaluation of complaints, including adverse events, and any required actions to correct and prevent a recurrence.

2.2 Activities and practices
What activities and practices were needed for successful post-market surveillance?
In several project countries, instrument operators and other healthcare facility staff were oriented and trained in post-market surveillance. In addition, the quality and performance of instruments and testing cartridges were monitored through site monitoring visits and connectivity. Designated staff consulted the online dashboard to view each machine remotely and analyze the results of each test performed by the operator. Typically, they consulted the dashboard at the start and end of each working day.

Trends in IQC failure rates were monitored and upward trends were investigated. Investigations included identifying root causes of IQC failures and proposing a collective action to reduce those failures. Serious events, such as batches of testing cartridges that produced higher than average IQC failures, were reported to WHO's Pre-qualification of In-Vitro Diagnostics Program (WHO-PQ) and the manufacturer.

2.3 Key implementers and collaborators

Who were the key implementers and collaborators?
In addition to end-users and health care providers, manufacturers of WHO prequalified IVDs are closely involved in the post-market surveillance process through their obligation to follow WHO "post-market surveillance of in vitro diagnostics." EGPAF and MOH staff, typically from the HIV prevention unit, accessed connectivity dashboards.

Staff from the national reference laboratory also accessed the connectivity dashboard. Collaborators included national authorities (regulators and reference laboratories) and WHO.

2.4 Resources (human, financial and material)

What resources were needed?
Resources required for post-market surveillance included human resources to monitor instrument and testing cartridge performance, as well as the following tools:

- error and specimen rejection log (paper-based);

- error log (electronic tool);

- data point or dashboard to view IQC failures and instrument breakdowns (electronic tool);

- tools for complaint reporting;

- trainings in post-market surveillance for facility staff, instrument operators, and healthcare workers.

Financial resources were required to cover costs associated with communication fees, including cell phone airtime. Communication is an important element of post-market surveillance, allowing health facilities, the manufacturers' in-country representative and regional office, as well as the MOH, to keep in contact.

2.5 Results

What were the results?
After training in instrument operation and post-market surveillance, end-users could demonstrate proper storage of the test kits according to the manufacturer's instructions for use. Instrument operators were assessed for the way they handle and use machines according to the manufacturer's instructions. Overall, they were able to demonstrate competence, including information management. They also could identify problems, document problems, investigate problems and communicate them. Complaints were documented using information from the records with the product code, lot number, expiry date, storage, temperature, affected consignment as well as any affected users and measures taken. The end-user notified the manufacturer of all complaints related to the use of their product. The national regulatory agency and WHO were also notified.

When an upward trend of a specific type of IQC failure was identified, whether operator or machine-related, action was taken immediately. Post-market surveillance identified trends in IQC failures that were related to instrument or testing cartridge failures, which were not operator-related. Some complaints were contractual; for example, the product was not delivered on time or the shelf life was not the same as agreed. Some complaints were adverse, also referred to as "incidents." EGPAF observed irregularities in certain cartridges from one manufacturer, who subsequently replaced the cartridges generating the failure. In one case, the machine was defective and it was exchanged for a new machine. Manufacturers were obliged to report post-market information to relevant national regulatory authorities and to the WHO. Post-market surveillance allowed the manufacturer to improve the products.

2.6 Lessons-learned

What worked really well?
The use of error and specimen rejection logs helped to identify potential issues with POC EID instruments and/or testing cartridges, and good communication between implementers and manufacturers ensured that issues were addressed as quickly as possible. A pre-market assessment prior to entry into the market was a helpful way to provide information on the product's safety, quality, and performance.

What did not work well?
Lot verification should verify that each lot supplied continues to meet pre-defined standards for safety, quality, and performance, and that transport and storage conditions have been well controlled. However, it is difficult to enforce. Lot verification samples should be taken from different testing sites at different levels of the health system; however, it was sometimes easier to verify lots at the district or regional levels.

In some countries, there was only one manufacturer representative to respond to requests. For this reason, it could take three to four days before the representative visited a site. Some broken-down platforms experienced long downtimes because the in-country manufacturer support team did not contact the regional technical support team in time for online troubleshooting.

In some cases, it was observed that health facilities communicated first with the manufacturer about an adverse event prior to informing the MOH focal point and EGPAF, which made it a challenge to follow up.

2.7 Conclusions and recommendations

What recommendations can be made for those intending to adopt the documented activities and practices for post-market surveillance?
A focal point for post-market surveillance within the MOH should be identified and communication protocols established for healthcare facilities to follow when reporting adverse events with POC EID instruments or testing cartridges. Testing sites should be sensitized to quickly report any issue they may have with cartridge or platforms.

It is recommended to have good communication between the health care facility and the national post-market surveillance focal point. IQC failures should be closely monitored through the use of error logs and connectivity solutions. Upward trends in IQC failures should be investigated and the underlying causes identified. Manufacturer related IQC failures or non-adherence to contractual obligations by manufacturers should be reported to the national post-market surveillance focal point, who should in turn alert WHO-PQ and the manufacturer. Manufacturers should have sufficient exchange platforms at country level, and more than one representative available in each country in order to avoid long waiting times for the repair or replacement of non-functioning platforms.

3. Guidance, Tools and References

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

3.1 Guidance

1. Unitaid/EGPAF (May 2017). **Guidance Note on POC EID Site Monitoring.** Available in the POC toolkit: http://childrenandaids.org/node/985

2. Unitaid/EGPAF (October 2019). **Post-Market Surveillance of IVDs: How to Detect Issues on POC NAT Assays and When/How to Fill an IVD Complaint Form** https://www.pedaids.org/wp-content/ uploads/2020/02/Post-market-surveillance_POC-EID_Lemaire_Oct2019.pptx

3. Unitaid/EGPAF (October 2017). **Optimizing Early Infant HIV Diagnosis through the Introduction of Point of Care Testing. Post-Market Surveillance. Lesotho Case Study**. https://www.pedaids.org/wp-content/uploads/2020/02/Post-Market-Surveillance_Lesotho-Case-Study_11Oct0217.pptx

3.2 Tools

4. Unitaid/EGPAF (March 2017). **Site Monitoring Checklist: Stand-Alone Testing Site.** Available in the POC toolkit: http://childrenandaids.org/node/985

5. Unitaid/EGPAF (March 2017). **Site Monitoring Checklist: Hub Testing Site.** Available in the POC toolkit: http://childrenandaids.org/node/985

6. Unitaid/EGPAF (May 2017). **Site Monitoring Checklist: Spoke Testing Site.** Available in the POC toolkit: http://childrenandaids.org/node/985

7. Unitaid/EGPAF (April 2019). **Example Site Monitoring Visit Schedule and HR Analysis.** https://www. pedaids.org/wp-content/uploads/2020/02/Post-market-surveillance_POC-EID_Lemaire_Oct2019.pptx

8. ASLM, CHAI, EGPAF, UNICEF, Unitaid (2017) **Unitaid POC EID Testing Mentorship/Supervision Checklist.** Available in the POC toolkit: http://childrenandaids.org/node/990

9. Unitaid/EGPAF (November 2018). **Error and Specimen Rejection Log.** Available in the POC toolkit: http://childrenandaids.org/node/990

3.3 References

ASLM, CHAI, EGPAF, UNICEF, Unitaid (Nov. 2018). Point-of-care connectivity issue brief. Available in the POC toolkit: https://www.childrenandaids.org/node/897

World Health Organization (2015). Post-Market Surveillance of in vitro diagnostics. Available at: https://www.who.int/diagnostics_laboratory/postmarket/en/ [Accessed, 13 October 2019]

4. Acknowledgements

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