Viral Load and Early Infant Diagnosis (VL/EID) Implementation Subject Matter Experts (ISMEs) Reference Manual

VL/EID ISME Community of Practice

January 2019

Acknowledgements

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1.0 INTRODUCTION

PEPFAR nations and implementing partners have demonstrated significant progress over the past 15 years identifying many patients in need of ART and starting them on life-saving antiretroviral therapy (ART). An HIV viral load (VL) test measures the amount of virus in the blood, and therefore is a proxy for assessing the effectiveness of ART in controlling the virus; the UNAIDS 3rd HIV treatment target states that by 2020, 90 percent of patients on ART should be virally suppressed. However, measuring the VL of all patients on ART and acting upon these results in a timely manner remains a challenge in many national HIV programs. Similarly, uptake of early infant diagnosis (EID) by two months of age remains poor with only an estimated 66% of HIV-exposed infants tested by two months of age within PEPFAR supported sites in 2018 (1). HIV infection in infants is aggressive, with the highest morbidity and mortality occurring in the first few months of life for perinatally-infected infants not on treatment. Low access to both VL and EID testing coverage can jeopardize the ability to achieve the UNAIDS 90-90-90 targets by 2020 and needs urgent attention.

The VL/EID Implementation Subject Matter Experts (ISME) Community of Practice (COOP) is a group of experts from the PEPFAR community that includes clinicians, laboratorians, strategic information and supply chain specialists. The main objective of the COOP is to identify innovative tools, best practices and solutions to guide ISMEs and PEPFAR country teams to address gaps and accelerate VL and EID scale-up. The VL/EID ISME Reference Manual is one of the innovative tools to help drive this process.

The VL/EID ISME Reference Manual is a guide for ISMEs as they offer either in country or remote technical assistance in VL/EID scale-up. Collectively, it presents best practices and proposed solutions for the challenges that are common across PEPFAR programs. Some sections of this manual discuss VL and EID together where the issues are similar; in other sections, VL and EID are discussed separately due to unique considerations at the patient and facility level. The guidance in this manual cannot replace the hard-earned expertise and knowledge of the ISMEs or the skill of colleagues in the field, but it can help guide ISMEs as they work with countries on challenges that are beyond their area of expertise.

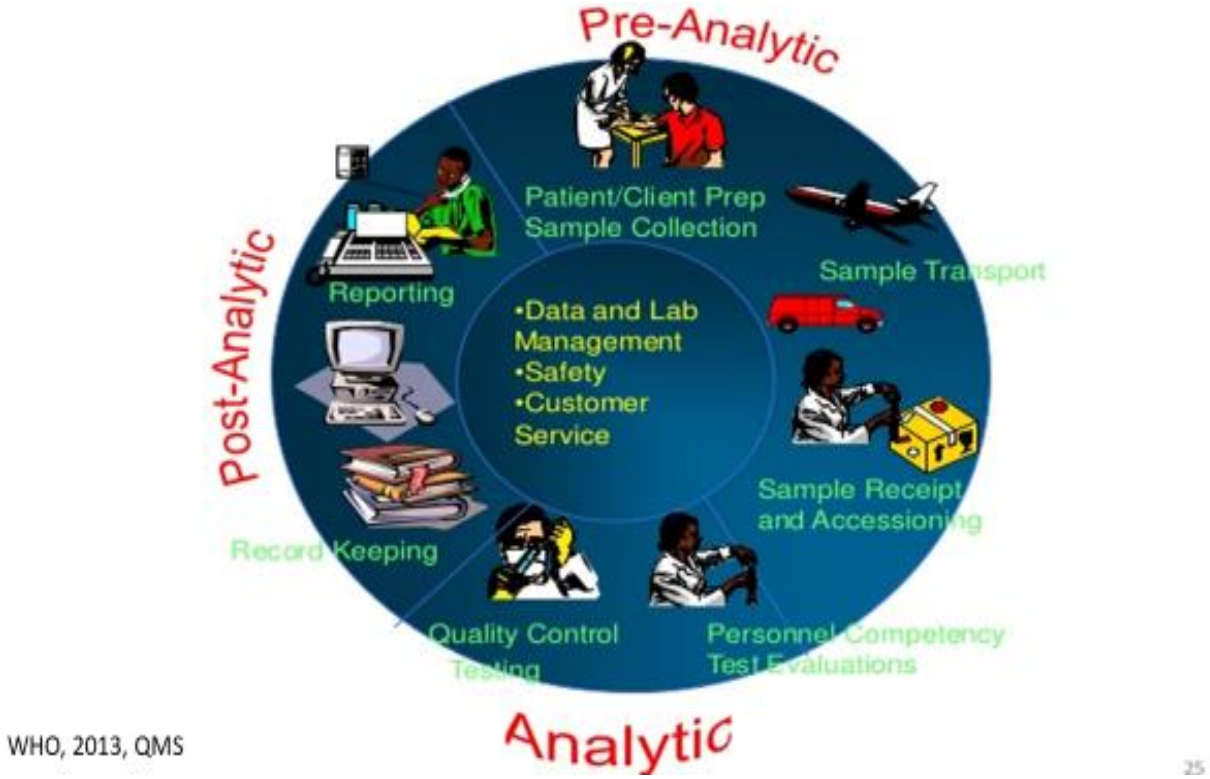
This manual is a living document and can help support the efforts of ISMEs and field colleagues to implement high quality, routine VL/EID testing for all patients on ART.

2.0 THE VL/EID DIAGNOSTIC CASCADE

The VL/EID cascade involves three distinct yet critically inter-dependent phases (pre-analytic, analytic, post-analytic) that span across health care facilities (clinics) and molecular testing laboratories, beginning with demand creation and ending with the utilization of results for patient care management. Gaps in the cascade yield negative consequences such as low testing coverage and long turnaround time (TAT) for return of results with subsequent late identification of and interventions for HIV-infected infants and management of viral non-suppression. Closing these gaps and accelerating access to VL/EID testing in PEPFAR supported countries will require concerted multi-pronged efforts to efficiently address challenges in each component of the diagnostic cascade. Figure 1 below from the WHO (2013) Laboratory Quality Management System manual shows an example of how countries can plan a well-structured diagnostic system.

This VL/EID Reference Manual presents common challenges in VL/EID testing across the three phases of the diagnostic cascade, starting with the pre-analytic phase. A section on "Cross-cutting Considerations" presents overarching topics that require national leadership and stakeholder involvement. For each issue, a list of tools is provided to identify or define the issue in countries, followed by a list of potential solutions to address the issue.

Figure 1: Phases of the Diagnostic Cascade



3.0 THE LABORATORY-CLINIC INTERFACE

A strong VL/EID Testing Cascade relies on a strong laboratory-clinic interface. Within the VL/EID testing network, laboratories and clinical facilities must coordinate efforts to ensure that critical steps of the cascade operate smoothly and efficiently. The collection of samples from health care facilities and transportation to VL/EID testing laboratories for processing is one example of direct interface between laboratories and clinics. The return of test results to facilities is another example of how the interface relies on close coordination and communication between facilities and laboratories. Communication between laboratories and facilities should be managed by designated focal persons at both the laboratory and facility. In many health facilities, there may need to separate focal persons for VL and EID due to different service delivery points (e.g., ART clinic for VL and PMTCT/ANC clinic for EID). Standard operating procedures should help focal persons and supporting staff navigate the details and processes of ensuring a smooth interface. While the interface is defined by specific points along the cascade, these critical steps determine the flow and successful completion of the entire VL/EID testing cascade.

4.0 VL/EID TOOLS

Below is a list of key resources and tools for VL and EID implementation; these tools are referenced in more detail within the technical sections of this resource manual (Sections 5-8).

1. **Clinical Facility VL Service Quality Tool (**https://www.pepfar.net/ect-m/isme/_layouts/15/start.aspx#/)
   Focused assessment of critical steps in the VL cascade, including the laboratory-clinic interface, documentation of VL results in patient files, and management of non-suppressed VL results.

2. **VL Scale-up Clinical Facility Readiness Assessment (**https://www.pepfar.net/ect-m/isme/_layouts/15/start.aspx#/)
   Comprehensive assessment and scoring of a facility's readiness and capacity to provide routine VL monitoring by documenting baseline situation and improvements in key components of the VL cascade

3. **HIV VL and Infant Virologic Testing (IVT) Scorecard (**http://www.aslm.org/hiv-viral-load-testing/hiv-viral-load-scale-tools/)
   Comprehensive assessment and scoring of laboratory activities for VL and EID services by documenting baseline situation and improvements

4. **Considerations for Developing a Monitoring and Evaluation Framework for Viral Load Testing (**http://www.aslm.org/hiv-viral-load-testing/hiv-viral-load-scale-tools/)
   Key considerations and examples of tools to assist countries in developing a national VL monitoring and evaluation plan.

5. **COP18 Laboratory instrument mapping spreadsheet** (https://www.pepfar.net).
   Spreadsheet to use in capturing and calculating instrument capacity.

6. **COP18 Laboratory instrument mapping outcomes data** (https://www.pepfar.net**).**
   Country instrument footprint obtained through the instrument mapping exercise.

7. **Laboratory Efficiency and Quality Improvement Tool (LabEQIP)**
   GIS-based tool that helps improve instrument placement strategies, referral network optimization, external quality audit (EQA) monitoring and performance review, and human resources coverage.

8. **Guidance for Developing a Specimen Transport and Referral System for VL and Infant Virologic HIV Diagnosis Testing Networks (**http://www.aslm.org/hiv-viral-load-testing/hiv-viral-load-scale-tools/)

Provides a systematic approach in developing a coordinated, standardized, reliable, efficient, cost-effective and sustainable specimen transport and referral system to support IVHD and VL testing networks.

9. **VL/EID Hub Assessment Form (**https://www.pepfar.net/ect-m/isme/_layouts/15/start.aspx#/)
   Focused assessment of the operational capacity of hubs to store, process and preserve the integrity of VL and EID specimens that are transported from facilities to testing laboratories.

10. **ForLab (Laboratory Commodity Forecasting Tool) (**https://github.com/forlab/ForLAB)
    Performs long- and short-term forecasts of commodities needs and guides improvements in diagnostic services.

11. **Pipeline** (Pipeline Monitoring and Procurement Planning System)
    (https://www.ghsupplychain.org/resource/pipeline-monitoring-and-procurement-planning-system)
    Assists program managers to plan optimal procurement and shipment schedules for health commodities and to monitor the stock status of health commodities.

12. **Supply Chain Guru (Llamasoft)**

13. **POC for EID Scale-up Solution document and Reference Manual** (https://www.pepfarsolutions.org/solutions/2018/11/6/increasing-access-and-coverage-of-hiv-1-early-infant-diagnosis-through-use-of-point-of-care-testing)

14. **HIV Point-of-care Diagnostics Toolkit**
    (https://www.childrenandaids.org/poc-toolkit-page)
    Includes:
    - Key Considerations document
    - Tools organized around four modules:
      - ✓ Product and Site Selection
      - ✓ Forecasting and Supply Planning
      - ✓ Regulations
      - ✓ Quality Assurance

15. **HIV-Exposed Infant (HEI) Care and Testing Toolkit**
    https://www.childrenandaids.org/HEI_Toolkit
    Includes:
    - Care of the HIV-Exposed Infant flipchart: counseling aid with key messages for HEI care and testing/EID
    - Dried Blood Spot (DBS) Job Aids for the clinic and laboratory
    - Videos on DBS collection for EID and VL: Training videos for health care workers available in English, French and Portuguese

5.0 KEY CONSIDERATIONS OF THE PRE-ANALYTIC PHASE

5.1 Demand Creation

Demand creation is an essential component of national scale-up of routine VL/EID testing. A lack of demand stagnates the development of VL/EID laboratory capacity, as low sample volumes can lead to inefficient use of laboratory resources or a delay in returning results. Demand creation strategies should involve patients, peer educators, counselors, and healthcare workers to ensure that all stakeholders are aware of the importance of early infant virologic testing for HIV diagnosis and routine viral load monitoring to optimize treatment outcomes.

5.1a Demand creation for Viral Load

Demand creation should ensure that stakeholders learn the differences between routine VL monitoring, CD4 monitoring, and targeted VL testing, understand the meaning of VL results, and know next steps for clinical management. Given the low uptake of repeat VL testing in patients with viral loads > 1000 copies/ml, special emphasis should be given to high VLs, ensuring results are returned to the patient and are utilized for clinical management. Demand creation for VL testing may be hindered when the return of results are delayed and clinicians cannot utilize results in a timely fashion; therefore, it is important to examine processes across all the phases of the VL cascade to ensure that clinicians and patients are able to respond promptly to VL test results.

Tools to identify the issue:
• Monitoring, Evaluation, and Reporting (MER) Guidance: TX_PVLS and TX_CURR indicators • VL Scale-up Clinical Facility Readiness Assessment • HIV VL and IVT Scorecard • National dissemination of training materials, or schedule of training for clinicians • VL/EID Patient education materials & job aids (Check for quality of content and availability of tools)
Suggested solutions:
• Engagement of peer educators and counselors in training and dissemination of information regarding routine VL testing, significance of results, and clinical management • Healthcare worker refresher trainings on VL/EID and high VL management in keeping with national HIV treatment guidelines • Educational materials tailored specifically for children and adolescents to help both patients and guardians understand the importance of VL monitoring • Engagement of community-based organizations to increase patient demand by promoting awareness and education of VL/EID testing and management of high VL

5.1b Demand creation for EID

Demand creation for EID should ensure that all stakeholders - in particular mothers, male partners and other caregivers - understand the importance of early HIV testing in infants, as well as the need for repeat testing during the period of exposure (breastfeeding) before determining a final HIV diagnosis at least three months after the complete cessation of breastfeeding. Education about EID and infant HIV testing should start early in antenatal care and be reinforced throughout pregnancy, delivery and breastfeeding. Providers must educate caregivers \ on the importance of returning to the facility to know EID results: HIV-positive infants can fall seriously ill very quickly if not started early on ART.As is the case with VL results, caregivers may be discouraged from following up on EID results if they are not ready at the scheduled appointments. It is important to ensure that both clinicians and caregivers are able to access and act on EID results in a timely fashion.

Tools to identify the issue:
• Monitoring, Evaluation, and Reporting (MER) Guidance: PMTCT_EID, PMTCT_HEI_POS, and PMTCT_STAT_POS indicators • National dissemination of training materials, or schedule of training for clinicians • VL/EID Patient education materials & job aids, including HIV-Exposed Infant Care and Testing flipchart (link in Section 4.0 #15)
Suggested solutions:
• Pro-active tracking to identify HIV-exposed infants of women enrolled in the PMTCT program: -Anticipate estimated date of delivery and follow-up with women who have not presented for delivery/ enrollment of HIV-exposed infant -Enroll HIV-exposed infants in the PMTCT program at maternity/birth and give follow-up EID visit date; use appointment register and active tracking of missed EID appointments • Education and identification of HIV-exposed infants outside of the ANC/PMTCT setting: maternal HIV status ascertainment in immunization clinics for HIV-exposed infant identification; PITC in high-yield entry points such as malnutrition clinics, inpatient wards and TB program • Use of peer educators (e.g., mentor mothers) for patient education about infant HIV testing and the comprehensive care of HIV-exposed infants, as well as client tracking -Example from PEPFARsolutions.org: Community focal mother model: Improving mother-baby pair retention in integrated maternal and child health and HIV services in Eswatini • Use of mother-infant pair clinic service delivery model to ensure coordinated care and education about the health needs of HIV-positive mothers and their HIV-exposed infants • Educational materials tailored specifically for pregnant and breastfeeding women and their male partners to help caregivers understand the importance of infant HIV testing and ongoing care

5.2 Incomplete laboratory requisition forms (LRF)

The ability to return VL/EID results to the correct health facility and match VL/EID results with the correct patients relies on the completion of the LRF without missing data. Data from the LRF allows programs to perform critical analyses including:

- Rates of VL suppression by age, gender, pregnancy or breastfeeding status, and ART regimen
- Proportion of VL tests performed by type of specimen collected (e.g., plasma versus dried blood spot (DBS), for specific reasons (e.g., routine VL monitoring, follow-up after enhanced adherence counseling, suspected treatment failure, etc.)
- Result of EID test and age at time of testing; reason for testing, whether initial or confirmatory test
- Turnaround time (e.g., time from sample collection to dispatch of results from the lab)
- Rejection rates

A national LRF for viral load and/or EID should contain key variables such as:

- Clinical facility name
- Patient name, unique ART number, date of birth, gender, pregnancy/breastfeeding status, date of current ART initiation, current ART regimen, ARV adherence
- VL or EID test order indication
- Sample type
- Requesting provider, date, contact information
- Date sample received by and results dispatched by the testing lab
- Rejection and reason

A facility-based SOP should be implemented that describes the steps for VL/EID test ordering, individual responsibility for completing the LRF, and facility-based procedures and monitoring to ensure that samples are not collected or leave the facility with missing/incomplete information.

Tools to identify the issue:
• VL Laboratory Requisition Form • EID Laboratory Requisition Form Clinical Facility VL Service Quality Tool
Suggested solutions:

- Standardized national LRF that captures key variables
- SOP at the facility for completing the LRF, including steps to ensure all fields are completed prior to samples being collected or leaving the facility
- VL and EID focal person(s) at the clinical facility who communicate with both clinical and laboratory staff
- VL/EID focal person at the hub and laboratory who communicates with the facility
- SOP at the laboratory for notifying the facility focal person(s) of missing/incomplete LRF fields, rejected samples, and/or delays in sample processing
- Facility monitoring of LRF completion issues and mentorship for improvement
- Oversight of the VL/EID testing lab-clinical interface to ensure functional and timely communication systems

5.3 Dried Blood Spot (DBS) Collection for EID and VL

Specimens for EID and VL may be collected using dried blood spots (DBS).

In DBS collection, small drops of whole blood are collected on strips of special filter paper, and the paper is then dried, packaged, and sent to a testing laboratory. The procedure for taking a DBS specimen for EID or VL involves obtaining blood with a lancet and applying it directly onto filter paper. For infants, blood is collected from the heel, toe or finger depending on age; for older children and adults, blood is collected from the finger.

Advantages of DBS testing include the following:

- A lower volume of blood is required for testing, so specimen collection is easier and requires less training
- DBS specimens have a longer lifespan than whole blood or plasma, are more stable and therefore easier to transport and store
- DBS specimen transport is easier than fluid specimen transport, allowing for shipment to distant laboratories without compromising the specimens
- Because specimens are dried, they pose little biohazard risk and are safer to handle than whole blood specimens

At sites where DBS is used for both EID and VL, it is important to keep EID and VL specimens separated to avoid cross-contamination. EID and VL should be dried in separate drying racks and packaged separately.

Tools :
• Job aids on DBS for both the clinician and the laboratory Available at: http://childrenandaids.org/HEI_Toolkit/DBS_Clinic_JobAid http://childrenandaids.org/HEI_Toolkit/DBS_Lab_JobAid • English DBS collection videos for EID and VL available at http://childrenandaids.org/index.php/HEI_Toolkit • English, French, and Portuguese DBC collection videos available at http://www.aslm.org/hiv-viral-load-testing/hiv-viral-load-scale-tools/
Suggested solutions:
• Special training for health care workers performing DBS collection with ongoing mentorship and supervision to ensure that quality samples are collected • Incorporation of training on documentation into training on DBS collection to ensure that health care workers provide complete and accurate documentation on laboratory requisition forms, logbooks, and other related tools • Focused mentorship for health facilities that have high specimen rejection rates or poor documentation Tracking the stock of DBS collection bundles and other related supplies to prevent stock outs and testing interruptions

5.4 Inadequate Sample Transportation Systems and Referral Networks

A sample transport system should enable all clinical facilities to refer samples for processing within the VL/EID testing network with a short turnaround time and clearly documented path for samples and results. The referral network should be planned according to the geographic distribution of the referring clinical facilities (lower sites) against the location of their respective intermediary collection facilities (hubs) and target VL/EID testing laboratories. Country programs should develop "double layered networks" with 1) an intra-district layer and 2) a provincial/regional/national layer. The weekly schedule for collection of samples from clinical facilities should be based on the schedule of VL/EID testing at facilities and frequency of contact with the hubs. Stakeholders should perform quarterly reviews of the feasibility of the weekly schedule for sample collection and of assigned roles and responsibilities. The means of sample transportation in each route and layer should be determined based on the distances traveled, cost, frequency of travel, and geography. Logbooks with individuals' signatures should track each point of transfer or responsibility in the sample referral network, including clinical facilities, intermediary hubs and VL/EID testing laboratories.

Tools to identify the issue:
• Up-to-date collection schedule for transporting samples from clinical facilities to intermediary hubs, and from hubs to VL/EID testing laboratories • Sample Transport Log book to review adherence to collection schedule, acknowledgement of sample collection by clinical facility staff, and actual distances traveled • Quarterly minutes or reports of VL/EID sample volumes routed from clinical facilities to intermediary hubs in the previous quarter and forecasts of expected volumes in the next quarter • Sample transport guidelines that define roles and responsibilities and key M&E indicators • VL/EID sample collection log at clinical facilities that documents rejection of samples and TAT for return of results • VL/EID log at laboratories that documents samples that were rejected (not processed) and TAT for dispatch of results • Guidance for Developing a Specimen Transport and Referral System for VL and Infant Virologic HIV Diagnosis Testing Networks • VL/EID Hub Assessment Form • LabEQIP to review existing sample referral and sample transport networks
Suggested solutions:
• Draft and share an SOP(s) for collection and receipt of results that documents each step at every level in the referral network (clinical facility, intermediary hub, VL/EID testing laboratory) and the roles of facility and laboratory points of contact and couriers • Share a weekly schedule for sample collection with names and phone numbers of points of contact at each clinical facility and laboratory, and the courier • Develop a sample tracking log with triple carbon copies that starts with documentation of sample collection from the clinical facilities, followed by a copy for the intermediary hubs

to document sample receipt and dispatch, followed by a copy for the VL/EID testing laboratory to document receipt of the sample.

- Implement bar codes to identify each patient sample and track it through the referral network
- Assign transport focal persons at the intermediary hubs who communicate with both the clinical facilities and the VL testing laboratories
- Coordinate quarterly meetings for stakeholders from clinical facilities, intermediary hubs and VL/EID testing laboratories to review and optimize weekly schedules for sample collection (e.g. bike rider routes and schedules), address prolonged TAT or missing results, and forecast volumes of samples to be collected
- Enter transport and site information into LabEQUIP to run optimization scenarios to reduce cost and transport time

5.5 Prioritizing VL Monitoring of Pregnant and Breastfeeding Women

Pregnant and breastfeeding (PBF) women who have a high VL are at greater risk for transmission of HIV to their children. Interventions such as extended post-natal prophylaxis for the exposed infant and adherence support for the mother can be offered to PBF women with high VL, but women must know to ask for VL testing and clinicians must know to offer it in order for these services to reach those who need them. It is important to understand if and how a country program is offering optimal VL testing services to PBF women, from demand creation and education of stakeholders to prioritization of processing and return of results from the laboratory. The VL Requisition Form should have a field for clinicians to indicate that the sample is from a PBF woman so that the laboratory will prioritize its processing. Similarly, the VL result reporting form should indicate that the result is for a PBF woman so that the clinical facility can flag it for immediate clinical review and action.

Tools to identify the issue:
• VL Scale-up Clinical Facility Readiness Assessment Site level patient tracking tools & community outreach tools (e.g., Mentor Mothers registers) • HIV VL and IVT Scorecard • VL Requisition Forms (should identify a PBF woman, her age & ART regimen)
Suggested solutions:
• National guidelines with an appropriate emphasis on assessment of VL in PBF women and what to do with high VL results. These assessments may need to be more frequent than routine VL testing recommendations for the non-pregnant adult HIV population. • SOPs that outline workflows and designate equipment time slots that appropriately recognize and respond to the time sensitivity of processing a VL sample from a PBF woman. • Demand creation efforts with facility and community-based groups to inform providers, lab staff, and patients of the importance of performing a VL on PBF women. • PBF women sample tracking procedures (e.g., logs, facility and community focal persons for high VL, meetings to track PBF patients in need of a VL or follow up of results) with appropriate designation of POC's for implementation and quality assurance.

5.6 Prioritizing VL Monitoring of Children and Adolescents

As many countries approach achieving 90% viral suppression targets, age disaggregated data reveals a large gap in viral suppression among children and adolescents as compared to adults. PEPFAR viral suppression data from 2017 showed overall viral suppression rates below 70% for children and adolescents aged 0-19 while adults 20 years and older had suppression rates of 80% or higher. This difference is due in part to higher rates of pretreatment and acquired HIV drug resistance among children and also suboptimal pediatric HIV drug formulations and dosing, difficulty administering medications, and issues related to HIV disclosure. In order to bridge this gap in treatment outcomes, it is imperative that children and adolescents receive timely VL monitoring and prompt management of high VL results.

Tools to identify the issue:
• Age disaggregated review of national and site-specific pediatric VL data • Clinical VL Service Quality Tool, administered in pediatric and adolescent treatment centers • Site-level patient tracking tools and community outreach tools for pediatrics and adolescents • HIV VL and IVT Scorecard • National and site-specific data on turnaround time for pediatric and adolescent samples • VL mapping exercise • Appropriate placement of POC VL technology • Appropriate placement of DBS VL collection and technology • Review of country level pediatric drug resistance data • Review of DSD models of care available to pediatric and adolescent patients
Suggested solutions:
• VL sample collection log at the facility in pediatric and adolescent treatment centers • VL focal person within the pediatric clinic (if pediatric clinic is in a different than that of the adult clinic focal person) • VL focal person at the laboratory who communicates with the facility • SOP at the facility for completing VL sample collection log (both at the time of sample collection and return of results) • SOP at the laboratory for notifying the facility of rejected samples and/or delays in sample processing • SOP at the facility for documenting receipt of results at the facility • Enhanced oversight and/or mentorship of VL lab-clinical interface at clinical facilities and laboratories • Introduction of DBS and/or POC VL technology to improve VL coverage and timely return of results • SOPs for active management of VL to ensure timely EAC and switch to 2nd line • Inclusion of pediatric and adolescent patients in DSD models • Provision of adolescent friendly services • Coordination of VL sample collection hours and location with pediatric and adolescent clinic hours and operations

5.7 Improving Key Population (KP) Access to and Uptake of VL Monitoring Services

While Undetectable = Untransmittable ("U=U") advocacy efforts have made great strides in treatment initiation and retention amongst PLHIV, their reach has been limited. Uptake of VL services among KPs remains limited due to multiple reasons, including stigma and limited understanding of the value of suppressed VL. Few KP programs provide treatment services, and staff at most general population treatment facilities are not trained to work with KP. Consequently, they do not ask if a person is a KP and if they do ask, KP may not be willing to identify themselves. This stigma further hinders the collection of KP-disaggregated viral load results. Improving KP access to and uptake of VL monitoring necessitates recognition of who they are and what risks they face, plans to monitor them over time, and delivery of differentiated services as needed. It also requires demand creation for VL monitoring from KP so that KP know to ask for VL testing if not offered to them and return to the clinic to obtain their viral load results.

Tools to identify the issue:

- Surveys that measure KP awareness of Knowledge, Attitudes and Practices (KAPs) towards VL monitoring and uptake
- VL Registers to assess if KP status is documented
- Individual High VL or EAC forms in patient charts to assess if KP status is documented

Suggested solutions:

- Referral mechanisms between KP programs and KP-friendly HIV treatment facilities to ensure KP are linked to facilities that measure VL and follow up with patients
- KP program staff educate and encourage KPs to go to KP-friendly HIV treatment facilities for VL monitoring
- KP sensitization and gender and sexual diversity training for laboratory and treatment facility staff
- Baseline measurement of VL monitoring and uptake across KP in all treatment programs and follow-up of trends over time as VL scale-up expands
- VL registers and other data collection tools with data fields specific to KP
- Linkage of KP-friendly facilities that provide treatment with the national VL network so that VL specimens from KP are processed and results are returned in a timely manner
- Monitoring of KP patients to ensure they return for VL results and provision of individual patient follow-up as needed
- Where feasible, provision of outreach VL monitoring services to accommodate drop-in centers and hot spots, with adequate clinical follow up in collaboration with affiliated treatment facility team
- Monitoring of KP viral suppression at treatment facilities in comparison with general population in order to identify if differentiated services are needed to support viral suppression among KP

6.0 KEY CONSIDERATIONS OF THE ANALYTIC PHASE

6.1 VL/EID Equipment Breakdown

Laboratory equipment breakdown constitutes a major bottleneck in the smooth running of laboratory and program services. It decreases productivity in the laboratory and delays the reporting of results for appropriate patient management. Several reasons can account for equipment breakdown including non-adherence to manufacturer recommended standard operation instructions, undertrained and/or untrained staff, unstable electrical supply, and lack of routine preventive maintenance contracts and/or service agreements. Once a piece of equipment has been installed and validated, laboratory staff need to establish and implement a plan for calibration, performance verification, and proper functioning of the instrument as well as ensuring appropriate documentation procedures in instrument logs. Furthermore, it is important to train and certify users of the equipment, comply with routine preventive maintenance, and ensure operational functionality and safe use. It is critical to establish service agreements that hold manufacturers responsible for repairing equipment breakdown. The routine monitoring of each instrument using key performance indicators, or KPIs (including error rates and causes, response and repair time, date of equipment breakdown, notification date of breakdown, repair date, etc.) should be included in maintenance contracts and service agreements, and reviewed regularly to assess overall functionality and the responsiveness of the manufacturer or third-party supplier to equipment breakdown.

Tools to identify the issue:
• Instrument preventive maintenance logs • Records of assay error rates and frequency of operator versus instrument errors • Documentation (logbook) of power outages and power fluctuations • HIV VL and IVT Scorecard
Suggested solutions:
• SOP for maintenance and operation of equipment • Training or refresher training and certification of instrument users • Manufacturer training and capacity building of in-country engineers to quickly repair or triage equipment problems for manufacturer repair • Implementation and regular review of routine preventive maintenance logs (daily, weekly and monthly reviews) • Connection of facility or instrument to power outlet through a surge protector • Connection of instruments to an adequate uninterruptable power supply (UPS) which is regularly maintained and serviced • Negotiation of reagent mark-up procurement strategy with manufacturer clearly being held responsible for repair • Reliable service agreement with manufacturers, monitoring of performance and documentation of response times, and adherence to all service and maintenance visits • MOU for a back-up testing laboratory and back-up patient sample storage in case of power supply issues, reagent stock outs and/or prolonged instrument down time

6.2 VL/EID Specimen Backlog

An efficient laboratory workflow ensures that specimens received in the laboratory are tested within the established laboratory turnaround time and results are returned to health care providers and their patients in a timely manner. Specimen backlogs can occur when there is suboptimal workflow in the laboratory network. For instance, a specimen backlog can be the result of poor sample quality, reagent or consumable stock out, equipment breakdown, underutilization or overutilization of the testing instrument, unreliable sample transport, staff shortages, and lack of appropriate laboratory management and oversight. Specimen backlogs strain the workflow of a laboratory, often leading to incorrect storage of patient samples due to limited freezer and/or refrigerator storage capacity. Furthermore, inventory management may be affected due to fluctuating demands of reagents and consumables, and in turn preventing the timely release of results and data entry. Optimizing laboratory testing efficiencies requires dedicated well-trained laboratory staff who can help prevent specimen backlogs by identifying potential issues before they lead to negative consequences. Laboratories should develop contingency plans for handling specimen backlogs, including consideration of additional shifts and referral of specimens to other facilities, depending on the cause of the backlog.

Tools to identify the issue:
• Performing regular inventory of reagents and consumables • Monitoring of reagent consumption to avert reagent stock out and/or reagent wastage • Equipment breakdown logs • Instrument inventory and utilization capacity • Documentation of power outages and power fluctuations • HIV VL and IVT Scorecard • Log of return of VL and EID results (at clinical facility and laboratory) • National turn-around-time data
Suggested solutions:
• Contingency plans, such as MOUs with back-up laboratories, in the event of a specimen backlog • Mapping an efficient sample workflow in the laboratory • Implementation of additional work shifts to clear backlogs • Training of laboratory staff on laboratory specimen backlog contingency plan and establishing focal person(s)responsible for preventing backlogs and responding appropriately • Procurement of additional instruments if demand for VL/EID tests exceeds the capacity of existing instruments, or upgrade to a higher throughput instrument if infrastructure and funding permit • Implementation of routine preventative and curative maintenance contracts • Monitoring of continuous quality improvement, including seeking laboratory accreditation • Backup generators for laboratories, or connection of alternate power supply and all critical pieces of equipment to an adequate uninterrupted power supply

6.3 Laboratory Network Optimization and Underutilization of Instruments

Lack of coordination among stakeholders has resulted in the procurement of more instruments than needed, stock-outs of reagents, and suboptimal VL testing coverage. The PEPFAR supported COP 2018 Laboratory instrument-mapping exercise showed that laboratory-based and point of care (POC) instruments are significantly underutilized. Despite this, country programs continue to request the procurement of more instruments without addressing the appropriate placement and optimal use of existing ones. Before requesting more instruments, country programs need to review their data from this exercise and conduct a full laboratory network optimization exercise (if none exists) to ensure appropriate and efficient sample transportation, supply procurement, placement and utilization of instruments to meet program needs within the context of the national tiered laboratory network. Purchase of POC and laboratory-based instruments without appropriate strategic planning has resulted in many problems, including instrument downtime resulting in backlogs and long turnaround times because of inadequate or poorly serviced maintenance contracts. To address these shortcomings, country programs should avoid outright purchase of laboratory instruments and explore the reagent rental or all-inclusive approaches that will promote shared responsibility between manufacturers and stakeholders, improve efficiency, and reduce testing interruptions. Laboratory network optimization needs in-country leadership with an appointed focal point and annual review of country instrument footprints and utilization.

Tools to identify the issue:
• COP18 Laboratory instrument mapping spreadsheet (https://www.pepfar.net) • COP18 Laboratory instrument mapping outcomes data (https://www.pepfar.net) • LabEQIP (Laboratory Efficiency and Quality Improvement Planning) • HIV VL and IVT Scorecard
Suggested solutions:
• Laboratory Network Optimization focal points at ministry level as well as among USG team members • Annual review of instrument footprint at national level • Engagement of diagnostic manufacturers on reagent rental or all-inclusive agreements • Service contracts with manufacturers of laboratory equipment • Availability and use of electronic instrument and reagent inventory systems • Training on instrument and reagent inventory management

7.0 KEY CONSIDERATIONS OF THE POST-ANALYTIC PHASE

7.1 Management of Return of Results from the Laboratory to the Clinical Facility

The return of results to clinical facilities relies on both clinical facility and laboratory teams' tracking the report of results for every VL/EID sample collected at the facility. The facility should keep a real-time log of every VL/EID sample that is collected from every patient, with the date of sample collection (VL/EID sample collection log). At least one staff member (e.g., the VL/EID focal person) should be responsible for checking that a result is returned for every sample that is collected, and for documenting the date of result return to the facility. The laboratory should also document the date that the facility receives the results. There should be a standard protocol for the facility to contact the laboratory if results from patients are not returned within the standard turn-around-time (ideally, within 2 weeks). Similarly, there should be a standard protocol for the laboratory to contact the facility if there are delays in returning results or if a sample is not processed.

Tools to identify the issue:
• Clinical Facility VL Service Quality Tool • VL Scale-up Clinical Facility Readiness Assessment • HIV VL and IVT Scorecard • National turn-around-time data • VL/EID testing platform mapping exercise (e.g., COP 2018 Laboratory instrument-mapping exercise)
Suggested solutions:
• VL/EID sample collection log at the facility • VL/EID focal person at the facility who communicates with the laboratory • VL/EID focal person at the laboratory who communicates with the facility • SOP at the facility for completing VL/EID sample collection log (both at the time of sample collection and return of results) • SOP at the laboratory for notifying the facility of rejected samples and/or delays in sample processing • SOP at the facility for documenting receipt of results at the facility • Enhanced oversight and/or mentorship of VL lab-clinical interface at clinical facilities and laboratories

7.2 Utilization of VL/EID Results at the Clinical Facility

Optimizing the lab-clinic interface impacts the utilization of VL/EID results in critical ways: returning VL/EID results with a short turn-around-time for return of results, matching results with the correct patient through the use of unique identifiers, and reporting VL/EID results in a standardized format that clinicians can interpret. The threshold and terminology used for reporting an undetectable VL result should be consistent across all reporting forms and clinical and laboratory facilities in the national program (e.g., <1000 vs <400 vs <20, or "undetectable" vs "target not detected"). VL/EID results need to be filed in patients' charts (electronic and paper) as soon as possible so that providers do not miss an opportunity to see the results and make decisions that impact patient management.

Clinicians need to know how to interpret a VL value and manage the patient's care based on the VL result. They should have access to VL training and job aids. Patient charts should have fields for documenting VL results and management plans. Providers need to know how to communicate the VL result to the patient, either to reinforce good adherence and refer to differentiated models of care if the VL is suppressed, or to discuss the importance of adherence and refer to counseling if the VL is non-suppressed. Providers should document the date of discussion, the next steps in the patient's treatment, and the date that the patient is due for the next VL test. Patient education materials can help providers with effective communication and improve patient literacy and patient demand for VL testing and results.

Similarly, EID results need to be documented in HIV-exposed infant registers and reporting of positive/indeterminate results back to caregivers must be prioritized over negative results so that HIV-infected infants can be initiated on lifesaving ART as soon as possible. (See next section on management of positive/indeterminate EID results.)

Tools to identify the issue:
• VL/EID Result Reporting Form • Clinical Facility VL Service Quality Tool • VL Scale-up Clinical Facility Readiness Assessment • High VL Register • Patient charts (electronic and paper)
Suggested solutions:
• Standardized VL Result Reporting Form • VL/EID focal person at the facility who communicates with the laboratory • VL/EID focal person at the laboratory who communicates with the facility • VL/EID job aids (posted algorithms, SOPs) • Patient education materials that explain the significance of a VL result • SOP at the facility for documenting receipt of results at the facility • SOP at the facility for management of return of results at the facility (flagging non-suppressed VL results, filing VL results in patients' charts) • Oversight of lab-clinical interface to ensure consistent, standardized reporting of VL/EID results

- Trainings and refresher trainings for clinicians on the significance and interpretation of VL/EID results

7.3 Management of Positive and Indeterminate EID Results

Receipt of a positive EID or IVT requires rapid action for timely linkage to ART, because perinatally-infected infants have a 35% chance of mortality by 12 months, which increases to 53% by 2 years of age. EID testing laboratories should prioritize the return of positive EID test results to facilities, and facilities should have a process in place to fast-track the results to the provider and urgently contact the child's mother and/or caregiver(s) to enable prompt initiation of ART. ART should be started without delay, and at the same time, a second specimen should be collected to confirm the initial positive virological test result for both conventional and point of care (POC) instruments.

Confirmatory testing in the event of a non-negative result (positive or indeterminate) is critical due to the risk of low-level viremia; possible contamination with maternal blood; specimen mislabeling, or laboratory contamination. The WHO recommendation to repeat testing of all indeterminate results to avoid errors in test results classification, is currently feasible only with the Roche platforms for which the indeterminate range has been established (13). WHO is currently working with other instrument manufacturers to establish similar indeterminate ranges. While this process is ongoing, PEPFAR recommends that all samples tested initially POSITIVE, including target detected with low and high signals, be repeated immediately using the same sample for all conventional instruments. A follow-up confirmatory test of all initial positive test results should be done using a new sample before or at the time of treatmentinitiation. Repeat testing of the same sample may not be possible with POC or near POC technologies when the sample is directly applied from the heel to the cartridge; however, in such instances, a new sample should be collected and immediately tested to confirm a positive test result and treatment should be initiated.

Tools to identify the issue:
• HIV-exposed infant registers • DBS tracking registers • Patient charts (electronic and paper)
Suggested solutions:
• Standardized EID Result Reporting Form • EID focal person at the facility who communicates with the laboratory • EID focal person at the laboratory who communicates with the facility • Oversight of lab-clinical interface to prioritize return of positive and indeterminate EID results • Positive EID register to track all HIV-infected infants to ensure linkage to ART • Patient education materials that explain the significance of a positive or indeterminate EID result • Trainings and on-site mentorship for providers on the significance of an indeterminate EID result, need for repeat and confirmatory testing • SOP at the facility for management of return of results at the facility (assigns responsibility for flagging positive and indeterminate EID results, communicating with providers, and filing EID results in patients' charts) • SOP at the facility for management of infants with positive or indeterminate EID results (contacting patients and urgently following up, tracking next steps)

- Patient/peer educators to support caregivers/mothers of HIV-exposed infants until determination of final outcome even after the first EID

7.4 Management of Non-suppressed VL Results

Non-suppressed VL results require urgent action because patients with non-suppressed VL are at risk of progression of HIV disease, transmission of HIV, as well as accumulation of HIV drug resistance mutations with lower chances for re-suppression on 1st or 2nd line therapy. VL testing laboratories should prioritize the return of non-suppressed VL results to facilities and facilities should have a system of immediately notifying providers to take action. Clinicians and adherence counselors need to have training and mentorship to understand the significance of non-suppressed VL values and next steps in the management of the patients' care. The time to complete each step in patient care should be documented and monitored, from the date of VL sample collection to the date of return of result to facility to the date that the VL result was shared with the patient. Patients with non-suppressed VL need to be tracked and followed closely to ensure that they receive timely interventions in care, such as enhanced adherence counseling (EAC), follow-up VL testing after improved adherence, and potential switches to new ARV regimens. Providers need tools and training to deliver high quality EAC that identifies and addresses adherence barriers. All steps in the management of non-suppressed patients, including plans and outcomes of adherence counseling, should be documented in individual patients' charts.

Tools to identify the issue:
• VL Result Reporting Form • Clinical Facility Service Quality Tool • VL Scale-up Clinical Facility Readiness Assessment • Patient Registers (ART Patient Register, and High VL Register) • Patient charts (electronic and paper)
Suggested solutions:
• Standardized VL Result Reporting Form • VL focal person at the facility who communicates with the laboratory • VL focal person at the laboratory who communicates with the facility • High VL Register and/or EAC Register that longitudinally tracks each step in the management of patients • High VL/EAC patient forms that are filed in patients' charts • Daily check of patient visit/EAC roster to flag missed appointments • VL job aids (posted algorithms, SOPs) • EAC job aids (flipcharts for providers to help identify and address patients' adherence barriers) • Patient education materials that explain the significance of a non-suppressed VL result • SOP at the facility for management of return of results at the facility (assigns responsibility for flagging non-suppressed VL results, communicating with providers, and filing VL results in patients' charts) • SOP at the facility for management of patients with non-suppressed patients (contacting patients and urgently following up, tracking next steps) • Stickers on charts/color-coded files of patients with non-suppressed VL • Oversight of lab-clinical interface to ensure timely return of non-suppressed results • Trainings and on-site mentorship for providers on the significance of a non-suppressed VL, management of non-suppressed patients, and high quality EAC

- Case managers for patients with non-suppressed VL
- Patient/peer educators to support patients with non-suppressed VL

8.0 KEY CROSS-CUTTING CONSIDERATIONS

8.1 Use of Point of Care (POC) Instruments to Support EID, VL and TB Testing

Current EID and HIV treatment cascades use laboratory-based instruments, requiring that samples (and results) travel long distances, resulting in prolonged turnaround time (TAT) and limiting access to testing. However, recent multi-country studies using POC testing to support EID scale-up have resulted in shorter TAT for return of results to caregivers, increased ART initiation rate and improved retention amongst HIV-exposed infants (2,3). WHO prequalified the use of two POC platforms (Cepheid GeneXpert® and Abbott m-PIMATM) to support EID and VL(4). The Cepheid GeneXpert® is a polyvalent platform that is also used for TB diagnosis. PEPFAR COP18 guidance indicates that country teams may use POC for EID where appropriate and as part of the conventional EID network. The PEPFAR VL/EID ISME Community of Practice has developed a Solutions document on the use of POC instruments for EID scale-up. The guidance in these documents should be adapted for each country's specific context in order to accelerate laboratory optimization and POC testing for EID. Although the importance of routine VL monitoring for HIV-infected individuals on ART is widely recognized, there has been minimal attention to VL monitoring in pregnancy and the postpartum period, particularly using point of care platforms that has potential to increases access to testing among these populations. In light of this and in order to optimize time-sensitive VL monitoring among PBFW, PEPFAR programs should plan to use POC for VL testing ONLY among PBFW. The TB community should be engaged at the national level to support strengthening and coordination of TB/HIV laboratory capacity integration to ensure efficient use of POC platforms. Country team engagement with partners (including the Ministries of Health, UNITAID, CHAI, and EGPAF) is necessary to address issues around supply chain, instrument placement & network optimization, connectivity, transition plans to local partners and governments, and data reporting and utilization.

Tools to identify the issue:
• POC for EID scale-up Solution document (https://www.pepfarsolutions.org/solutions/2018/11/6/increasing-access-and-coverage-of-hiv-1-early-infant-diagnosis-through-use-of-point-of-care-testing) • POC for EID scale-up Reference manual (https://www.pepfar.net/ect-m/isme/_layouts/15/start.aspx#/) • HIV VL and IVT Scorecard • VL and EID Quarterly Monitoring Tool • HIV Point-of-care Diagnostics Toolkit http://childrenandaids.org/index.php/poc-toolkit-page
Suggested solutions:
• In-country focal persons or points of contact, including clinical (HIV and TB) and laboratory colleagues, for EID/TB discussions and coordination • Integration and policy document to support laboratory optimization for EID (including conventional and POC) at national level

- SOP detailing POC for EID rollout process and subsequent handoff of network to local partners and governments

8.2 Long Turn-Around-Time (TAT) from sample collection to return of results to the clinical facility

Long TATs are associated with delays at any point along the cascade, from sample collection to receipt of results at the clinical facility. In order to improve TAT, systems must be strengthened and monitored in each phase of the testing cascade. VL/EID technical working groups (TWGs), lab-clinical teams, and VL/EID coordinators need to evaluate the referral networks against existing VL/EID lab capacity, balance the workloads at the different stages of sample management, and define standard cut–off times that should to be adhered to. Examples of recommendations include: time from sample collection at facility to receipt at lab (TAT1) of 3 days with samples referred from a facility twice a week; time from receipt at lab to dispatch of results (TAT2) of 5 days where the lab's work load is matched to its optimal capacity; and time from dispatch of results to receipt at facilities (TAT 3) of 2 days where results are transmitted electronically to the facility immediately after testing. Implementation of specific-and feasible strategies that address challenges within the three phases should improve the TAT from sample collection to return of results at clinical facilities. In addition, it is important to track the time from the return of results to facilities to notification of patients and/or caregivers (for more details, please see Sections 7.3 and 7.4 for Management of Positive and Indeterminate EID Results and Management of Non-suppressed VL Results, respectively.)

Local solutions based on unique circumstances and existing infrastructure are strongly recommended and should be feasible to implement. The optimal use of tools and SOPs is encouraged; electronic tracking systems could be of assistance, if available. Most importantly, all VL/EID testing labs should have frequently scheduled meetings with the referral sites in their network to address any issues leading to delays in turnaround times.

Tools to identify the issue:
• Clinical Facility VL/EID sample collection log • Hub VL/EID register /tracking logs • VL/EID Laboratory workload registers • National turn-around-time data • VL/EID testing platform mapping and site networking documents
Suggested solutions:
• VL/EID focal person at the facility, who serves both clinical and laboratory staff • VL/EID focal person at the laboratory who communicates with the facility • SOP at the facility for completing VL/EID sample collection log (both at the time of sample collection and return of results) • SOP at the laboratory for collection from the facility, documentation of receipt at the laboratory and documentation of dispatch of results to the facility • Enhanced oversight and/or mentorship of VL lab-clinical interface at clinical facilities and laboratories • Regular lab-clinical interface meetings between VL/EID testing lab and referring facilities

8.3 Lack of or weak laboratory Information systems (LIS)/connectivity

The increasing demand for VL/EID performance data has led to the need to collect more indicators that reflect the performance of the testing cascade. One challenge is to develop a laboratory information systems (LIS) that can interface with existing VL/EID testing instruments and return timely results to facilities. LIS should generate and print VL/EID test result report forms. LIS requires software based systems that will record, manage and store bulky VL data in an organized format. The start-up and maintenance costs for LIS may be expensive, as it requires significant investments in infrastructure. While testing labs in several countries are currently operating with LIS systems, a common and persistent challenge is the incompatibility and lack of inter-operability with other existing VL/EID LIMS, or National VL/EID dashboards. Despite the fact that most VL/EID laboratories are located in urban or semi-urban areas, internet services are unreliable, thereby creating suboptimal conditions for VL/EID laboratories to host individual lab servers. LIS systems must be able to function off-line and update data upon resumption of internet connectivity. Various LIS vendors exists and offer products at different annual licensing fees, some of which can be prohibitive. High workloads and data traffic require full-time engagement or designation of "super users" – or information technology (IT) experts that are on-site to support day-to-day trouble shooting of the systems. Most countries have not yet recognized the importance of IT support for a well-functioning LIS.

Tools to identify the issue:
• Logbook of VL/EID dashboard that documents functionality of LIS • Logbook at laboratory of VL Requisition Forms (VLRF) and Results Reporting Forms • Logbook of commodities management • Logbook of power outages and power fluctuations
Suggested solutions:
• Daily or Weekly data quality checks of the VL/EID dashboard • Weekly review of VLRF Logbook and cross check with data that has been entered into LIS • Weekly review of commodities management logbook and cross check with data entered into LIS • Weekly review of power and/or internet outages to assess need to secure a reliable internet services • LIS reports and data extraction for improving program outcome • SOP at the facility for documenting receipt of results • SOP at the laboratory for dispatch of results

8.4 Strengthening VL/EID Monitoring and Evaluation (M&E) Tools and Systems

Effective VL/EID M&E systems must be able to track overall VL/EID testing coverage (e.g., number of patients on ART receiving VL test or number of HIV-exposed infants receiving EID), VL suppression outcomes, EID positivity, and client tracking/cascades for EID and VL.

Effective VL M&E systems must also be able to track non-suppressed clients, and create VL cascades for specific age/sex/sub-populations to monitor VL outcomes effectively. Strong M&E systems at and between sites and laboratories are essential for effective VL monitoring.

Country programs have made progress in developing or updating M&E plans, tools, and systems to review and use VL data. However, ongoing challenges exist:

- VL tools are not consistently updated or nationally implemented to adequately track VL
- Lack of standardized M&E tools to track non-suppressed patients
- Incomplete VL forms and inaccurate recording of VL results in patient charts
- VL data not always integrated into DHIS2 or other HMIS tools from sites; often getting VL data from separate LIMS
- Multiple, unlinked systems without unique IDs making it challenging to track individuals versus tests
- Lack of utilization and triangulation of data to track overall VL testing coverage and outcomes
- Inadequate M&E training and lack of supportive supervision of site staff on VL data collection and use

Effective EID M&E systems should be able to track: EID coverage, EID positivity, linkage of HIV-positive infants to ART, and final outcome ascertainment of HIV-exposed infants. While MER indicators and most national reporting systems are cross-sectional, outcomes for HIV-exposed infants are most accurately reported using birth cohort reporting. Many countries have developed HIV-exposed infant birth cohort registers to allow accurate tracking of infant from birth until final HIV diagnosis.

Where systems may have made substantial progress with addressing the challenges above, data quality is an issue that requires continued attention. Challenges include:

- Reporting on number of tests and outcomes, not number of individuals and outcomes
- Incomplete or inaccurate data (e.g., disaggregated data incomplete or inaccurate)
- Clarification of VL and EID indicator(s) definition

Tools to identify the issue:
• Considerations for Developing a Monitoring and Evaluation Framework for Viral Load Testing, Sections 1 & 2, and Appendices 2 & 3 • VL Scale-up Clinical Facility Readiness Assessment Tool • Monitoring, Evaluation, and Reporting (MER) Guidance • Quarterly site-level list of the VL eligible and VL tested patients against total ART volumes • IATT M&E Framework for ART for Pregnant and Breastfeeding Women Living with HIV and their Infants (provides key considerations for infant cohort monitoring)
Suggested solutions:
• SOPs for VL data collection, reporting, and use (see Considerations for Developing a Monitoring and Evaluation Framework for Viral Load Testing, Figure 3 for example) • Utilization of updated and correct forms and tools at sites, and training of site staff on completing forms • Reviews of recorded data (both when test is ordered and result is returned) for completeness, accuracy, and high quality • Clarification of data source for reporting PVLS (i.e., patient record or LIS); if LIS, assessment of why patient records from site are not being utilized • Reporting of VL data for individuals, not tests; review of VL testing data for individuals compared to those on ART eligible for a VL test to assess overall VL testing coverage and outcomes • Update of existing data quality protocols/SOPs, processes, and tools to incorporate key VL indicators and specify methodology for VL data quality checks; routine VL data quality checks • Infant birth cohort monitoring through registers or electronic systems in order to track infant enrollment in care, completion of first test by 2months of age, ongoing retention in care, and ascertainment of final HIV status For documentation of successful linkage of HIV-positive infants to ART, PMTCT programs should document not only referral to ART clinic, but also infant's ART number and date of ART initiation

8.5 Reporting PEPFAR MER indicators for VL and EID

8.5a Viral Load Indicator: TX_PVLS

The ability to report on the percentage of ART patients with a VL result documented in the medical record or laboratory record/information system (LIS) within the past 12 months with a suppressed VL result (<1000 copies/mL) on the most recent test relies on the ability to distinguish individuals from tests. The source of data that is recommended includes electronic or paper patient records to ensure patient results are de-duplicated and documented for patient management. Alternatively, if a clinical source does not exist or contain the needed information, LIS can be the source of TX_PVLS data, but this requires that VL results are linked with individual patients and their clinical records at the facility level. PEPFAR-supported countries should specify and explain the data source used to report on TX_PVLS. National guidelines should specify the intervals for routine VL monitoring and the intervals may differ by patient population (e.g., non-pregnant adults, children, pregnant/breastfeeding women); in addition, there should be specific guidance for VL monitoring and interventions for patients with high VL results (e.g., VL≥1000 copies/mL). National guidelines, estimated rates of viral non-suppression and VL testing capacity should be used to set TX_PVLS targets. The ability to distinguish between tests and individuals is critical to ensure that countries can track overall progress of VL testing coverage; comparison of the TX_PVLS denominator to the result for TX_CURR from 6 months earlier (i.e. two quarters prior) can provide a crude estimation of VL testing coverage.

Tools to identify the issue:
• TX_PVLS MER Indicator Reference Sheet • MER Indicator Training Videos, (accessible: https://datim.zendesk.com/hc/en-us/sections/200929315-MER)-video covering MER TX indicators, including TX_PVLS, expected to be posted in Oct. 2018 • Considerations for Developing a Monitoring and Evaluation Framework for Viral Load Testing, Sections 1 & 2 (http://www.aslm.org/hiv-viral-load-testing/hiv-viral-load-scale-tools/) • Clinical Facility VL Service Quality Tool • VL Scale-up Clinical Facility Readiness Assessment Tool
Suggested solutions:
• Standardized national VL requisition form (VLRF) with patient unique identifiers used in VL results reporting/tracking • SOP at the facility for completing VLRF including steps to ensure completeness of VLRF prior to the collection and transport of samples from the facility • SOP at the laboratory for notifying the facility of missing/incomplete VLRF information • Enhanced oversight and/or mentorship of facilities and implementing partners on data collection and reporting of VL indicators • Data quality assurance activities to align different data sources on the number of individual VL test results reported for TX_PVLS (e.g., ART register, patient files, electronic medical records and LIS)

- Routine target setting exercises for VL testing and TX_PVLS with involvement of clinical, laboratory, and strategic information experts and based on national guidelines, program data and plans for scale-up

8.5b EID Indicators: PMTCT_EID, PMTCT_HEI_POS, and TX_NEW<1

PMTCT_EID: This is used to report the proportion of infants born to HIV-positive women who received a first virologic test (sample collected) by 12 months of age. This indicator is disaggregated by the age of the infant at the time of sample collection, either between birth and 2 months or between 2 and 12 months of age. The sum of the two age disaggregates equals the number of infants with an EID sample collected within the first 12 months of life. This indicator does not report on test results; rather, it is an indicator that reflects service delivery (EID coverage) for HIV-exposed infants. EID coverage is calculated by using PMTCT_STAT_POS (number of new and known HIV-positive women identified at ANC1) as the denominator.

PMTCT_HEI_POS: This indicator is used to report the number of HIV-infected infants identified in the reporting period, whose diagnostic sample was collected by 12 month of age. It collects any first positive virologic test result of a specimen collected in the first 12 months of life. Thus, if an infant's test at 6 weeks was negative but his second virologic test before 12 months came back positive, this indicator would capture the positive virologic test result. This indicator is disaggregated by age—0-2 mo vs. 2-12 months of age at the time of sample collection (regardless of when the result is returned), as well as by whether or not the infant is initiated on ART (PMTCT_HEI_POS_ART). As such, if reported appropriately, this indicator allows for calculation of true linkage rather than proxy linkage using TX_NEW as the numerator.

TX_NEW <1: This indicator reflects the number of infants <1 year initiating ART within the reporting period. In theory, this number should be equal to or close to PMTCT_HEI_POS_ART, which reflects the number of infants <12 mo with a positive EID result initiated on ART.

Tools to identify the issue:
• MER Indicator Reference Guide Version 2.3 FY19 • MER Guidance v2,3 PMTCT (https://datim.zendesk.com/hc/en-us/articles/360017926471-Monitoring-Evaluation-and-Reporting-MER-Guidance-v2-3-PMTCT)
Suggested solutions:
• ICPI HEI Dashboard: Helps identify data quality issues around PMTCT_HEI_POS_ART vs. TX_NEW <1

8.6 Reagents Stock-outs/weak Inventory System

VL/EID scale-up is dependent on effective supply chain management in several ways, including: forecasting testing demand; ordering and placement of instruments, reagents and consumables; and ensuring functionality of instruments. Procurement of VL/EID reagents and consumables begins with quantification of need and the development of a forecast and supply plan. Generally, historical consumption data, and demographic and/or target-based forecasts guide procurement. Challenges throughout the supply chain can impact product supply or demand. For VL/EID scale up, production demands may outpace manufacturing capacity, leading to prolonged lead times until products are delivered. Site-level changes, (e.g. large increases in demand, equipment breakdowns, new and/or non-traditional service points), cause fluctuations in commodity needs. With global efforts to introduce point-of-care (POC) or near-POC instruments, consumption demands may shift from conventional platforms to POC instruments. Uptake of POC testing should be closely monitored (e.g., monthly or quarterly reporting) to inform supply plan adjustments due to unpredictable changes in commodity needs.

Finally, ensuring adequate service and maintenance of instruments, has been an ongoing challenge across PEPFAR-supported countries. To date, instrument and vendor management has been conducted on a per instrument basis, with limited national coordination. It is critical that country programs define and monitor services expected as part of service contracts with manufacturers, and they should manage and assess vendors and instruments based on a set of key performance indicators.

Tools to identify the issue:
• ForLab (Laboratory Commodity Forecasting) tool (https://github.com/forlab/ForLAB) • Pipeline (Commodity Supply Planning) tool (https://www.ghsupplychain.org/resource/pipeline-monitoring-and-procurement-planning-system)
Suggested solutions:
• Implementation of an annual national (inclusive of all donors) VL/EID quantification and forecast plan • Adherence to monthly or quarterly reporting to ensure adequate reagent supply at the site level • Reagent rental contracting to promote appropriate placement and function of instruments

8.7 Reagent Rental/All-Inclusive Approach

To improve pricing transparency, coordination, improved service delivery and cost efficiency, PEPFAR and key global laboratory stakeholders are endorsing an all-inclusive/reagent rental procurement model based on a network approach to laboratory development. The all-inclusive/reagent rental price model allows for global and national coordination and alignment of instrument management strategies (e.g. lease vs. purchase; bundled reagent/service maintenance pricing). In addition, it facilitates the introduction of innovative technologies and promotes data use to inform maintenance strategies and instrument placement to improve utilization and function via service contracts with manufacturers. The implementation of the all-inclusive/reagent rental model requires baseline mapping of public health networks, including the laboratory network with all functional instruments and utilization rates, facility-level testing demand, sample referral routes, and additional supportive systems. The all-inclusive pricing model has been discussed with all major molecular based manufacturers who are well-positioned and eager to assist in supporting the broader network requirements.

Tools to identify the issue:
• PEPFAR Lab Instrument Inventory tool • Laboratory Efficiency and Quality Improvement Tool (LabEQIP) – Network mapping and optimization • Supply Chain Guru (Llamasoft) • CHAI POC selection tool
Suggested solutions:
• Development of a systems/network approach to laboratory diagnostic services through a complete understanding of country data and related factors • Review of GIS data to understand laboratory instrument locations and patient testing demands • Efficient and integrated sample referral networks • Model of a POC integration strategy over the conventional network scale-up plan to determine placement approach • Pursuit of “all-inclusive” reagent rental/leasing models over purchase • Appropriate incorporation of POC diagnostics into the overall laboratory network. • Measurement of key performance indicators to ensure end user and instrument operability (vendor, instrument, and end user monitoring – with established thresholds)

8.8 National Coordination of VL/EID Scale-Up with a National Workgroup/Committee

National scale-up of routine HIV VL/EID monitoring requires stakeholders across multiple technical disciplines and programmatic areas to engage regularly in coordinated planning, monitoring, and communication of VL/EID scale-up activities and progress during implementation. Coordination of VL/EID scale-up at the national level through an interdisciplinary technical workgroup or other oversight body provides opportunities for technical experts and stakeholders across the clinical, lab, supply chain, community, and monitoring & evaluation program areas to collaborate and share updates on the progress of VL/EID scale-up. Stakeholders and implementing partners also have the opportunity to formalize relationships in a forum where they can share best practices or concerns that can provide early indications of problems at local or regional levels where interventions may be required. These relationships can be leveraged to strengthen laboratory network systems and strategically negotiate maintenance contracts with manufacturers and the purchase of VL/EID commodities.

Tools to identify the issue:
• Minutes or records of meetings of a national technical work group to determine if efforts to support VL/EID scale-up are effective & appropriately inclusive • Review of terms of reference to assess membership and operational functions of the workgroup
Suggested solutions:
• Regular meetings of an interdisciplinary workgroup including members representing clinical, laboratory, supply chain, and M&E program areas • VL/EID national coordinator with the role of facilitating regular communications, following up on action items from meetings, and coordinating implementing partners, MOH, PEPFAR and other donors, civil society, and other external stakeholders • 3. MOUs for implementing partners that outline their role in participating in the workgroup and interagency collaborations

8.9 The Undetectable = Untransmittable (U=U) Slogan

Scientific studies have provided evidence of zero risk of HIV sexual transmission from an HIV-positive to an HIV-negative primary partner during condomless anal and vaginal sex with the use of suppressive ART (5-8). The landmark HPTN 052 phase III randomized clinical trial showed the personal and public health benefits of early treatment referred to as Treatment as Prevention (TasP) (9). This clinical trial reported no linked HIV transmissions within serodiscordant couples having unprotected sex when the HIV-positive partner had durable viral suppression (9). In 2016, the Prevention Access Campaign launched the slogan Undetectable=Untransmittable (U=U), to raise HIV prevention awareness and decrease HIV stigma (10). Over 700 organizations from 100 country programs have taken up the message of U=U. The U=U goals are to eliminate the stigma associated with the negative association of PLHIV as disease vectors and generate demand for treatment through its promotion in clinical, community and other settings. This implies PLHIV who maintain repeatedly undetectable viral loads (defined as < 200 cp/mL) can live healthy lives without the fear of passing infection to their sexual partners (11). Since the messages of both TasP and U=U are important towards achieving the UNAIDS 95-95-95 fast-track targets, an understanding of how to incorporate and disseminate this evidence-based data to reduce HIV stigma, encourage individuals to seek and adhere to HIV treatment, and achieve and maintain viral suppression are needed. The utility of U=U in combating stigma and instilling greater hope for PLHIV provides a stronger impetus for ensuring access to routine VL monitoring, for identification of viral suppression, and early detection of viral rebound. Although current criteria for U=U is a VL result of less than 200 copies/ml, there are ongoing clinical trials and data analysis to determine if and at what level of viral detection HIV transmission can occur above the current 200 copies/ml cut-off. Some PEPFAR-supported countries have started or are planning to start the U=U campaigns for specific populations along with policy, prevention, care and treatment interventions. Considerations and implications for public health implementation (e.g., policy decisions, messaging for specific populations, laboratory testing, clinical and programmatic strategies) of U=U messaging need to be further explored in PEPFAR-supported countries.

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