Roche + CDC Partnership (ASLM Webinar)

Develop Capacity and Improve Efficiencies in Laboratory Operations

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February 11, 2021

Purpose and Disclaimer Slide

The purpose of this presentation is to provide information on tools developed in partnership with the CDC ILB to support continued scale up of HIV viral load and early infant diagnosis. These tools provide support training and implementation efforts and can contribute to improving laboratory efficiency and strengthening across the programs.

These tools will be available via the ASLM Resource Center for easier access online providing the ability to access them when it is in convenient for your lab, to provide you with updates for the latest innovations to support your HIV programs and to help reduce time spent to build training, implementation or other laboratory activities.

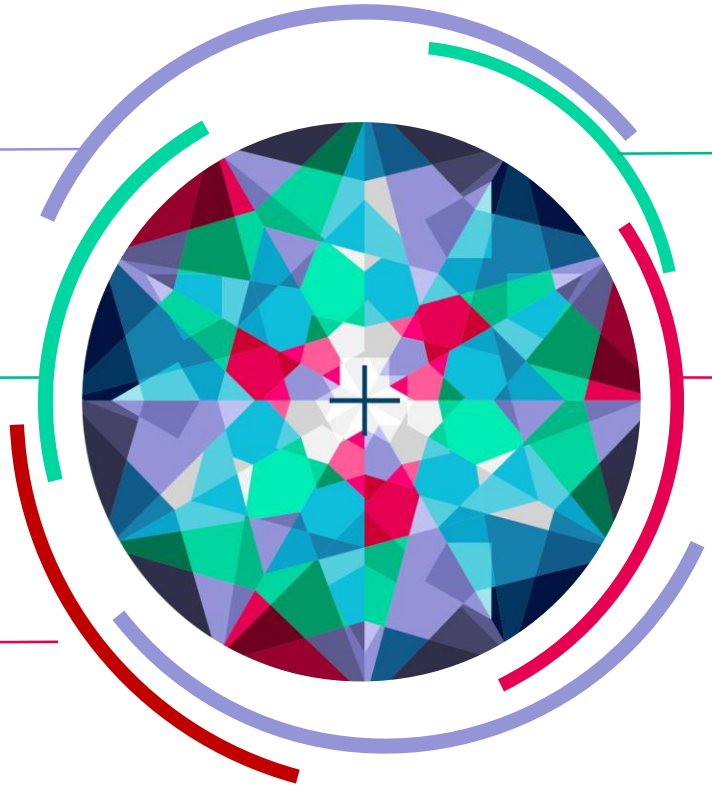
This information is shared for your awareness of their availability, location and content and does not reflect endorsement by ASLM.

Agenda

Introduction: Partnerships

Implementing cobas® Plasma Separation Card

Summary & Questions



Building Capacity on EID DBS to Enhance Access to testing

Streamlining Verification of Assays

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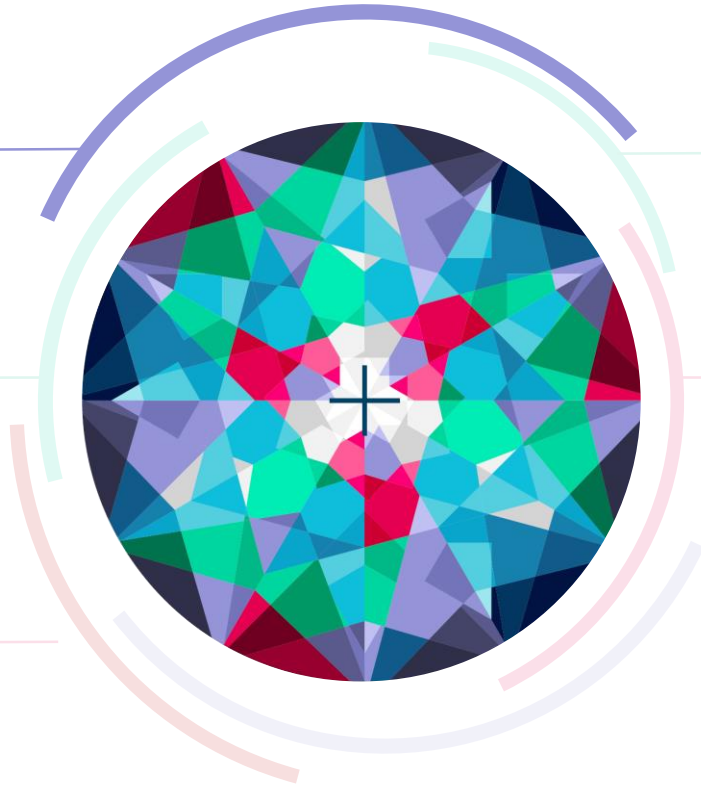


Public–Private Partnership (PPP) for HIV/AIDS Response

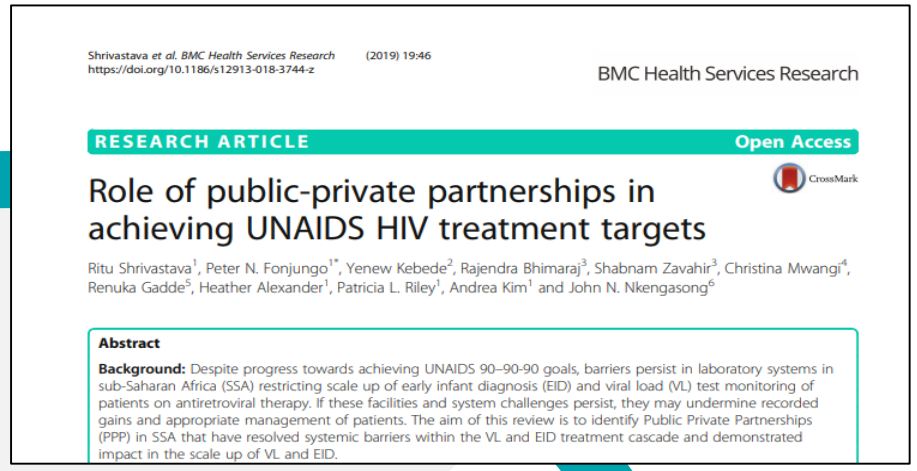
Developing laboratory tools for viral load and EID scale up

Menu Search Media

Roche and the US President's Emergency Plan for AIDS Relief (PEPFAR) partner to strengthen laboratories medicine training and knowledge on the African continent

Basel, 04 December 2012

Today Roche Diagnostics and the US President's Emergency Plan for AIDS Relief (PEPFAR) announced a public-private partnership to improve the capacity of laboratorians and strengthen laboratory systems in African nations highly impacted by HIV/AIDS. Valued at $12 million over five years, the goal of the partnership is to build institutional capacity of regional and national partners by developing certification programs for laboratory technicians, strengthening pre-service curricula, and institutionalizing quality improvement in diagnostics services.



Shrivastava *et al. BMC Health Services Research* (2019) 19:46
https://doi.org/10.1186/s12913-018-3744-z

BMC Health Services Research

RESEARCH ARTICLE Open Access

Role of public-private partnerships in achieving UNAIDS HIV treatment targets

Ritu Shrivastava[1], Peter N. Fonjungo[1*], Yenew Kebede[2], Rajendra Bhimaraj[3], Shabnam Zavahir[3], Christina Mwangi[4], Renuka Gadde[5], Heather Alexander[1], Patricia L. Riley[1], Andrea Kim[1] and John N. Nkengasong[6]

Abstract

Background: Despite progress towards achieving UNAIDS 90–90-90 goals, barriers persist in laboratory systems in sub-Saharan Africa (SSA) restricting scale up of early infant diagnosis (EID) and viral load (VL) test monitoring of patients on antiretroviral therapy. If these facilities and system challenges persist, they may undermine recorded gains and appropriate management of patients. The aim of this review is to identify Public Private Partnerships (PPP) in SSA that have resolved systemic barriers within the VL and EID treatment cascade and demonstrated impact in the scale up of VL and EID.

Improved laboratory capacity and accelerated training of lab staff

Quality improvement for laboratory services, including certification courses for molecular diagnostics & QMS

PEPFAR

Roche

CDC

ASLM

Developing pre-service training curricula

Collaboration with the ASLM to strengthen local capacity and to promote country ownership and sustainability

"PPP contributions to laboratory systems strengthening are a model"[1]

Source: https://www.roche.com/media/releases/med-cor-2012-12-04.htm. Accessed 5 Sept 2018

1. Shrivastava et al. BMC Health Services Research (2019); https://doi.org/10.1186/s12913-018-3744-z

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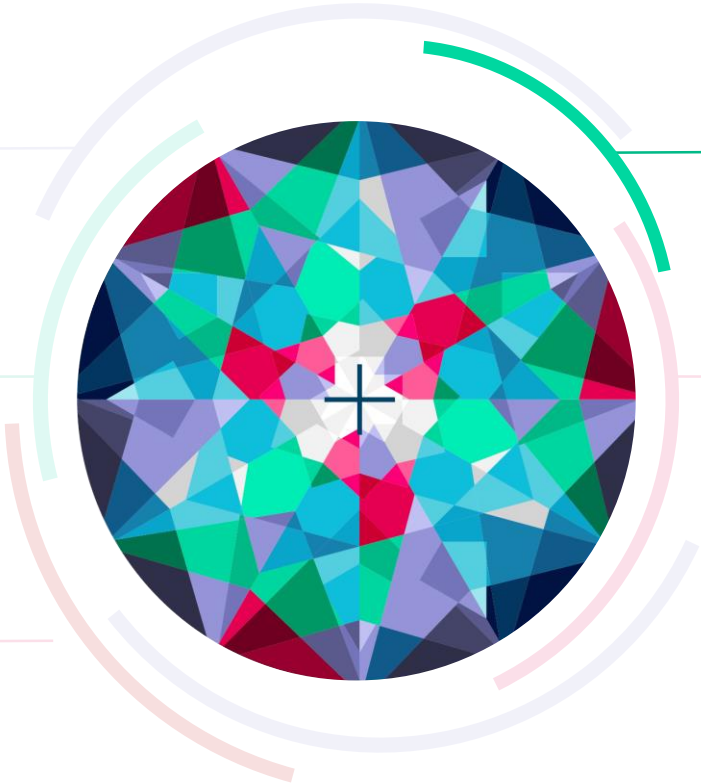

Building Capacity on EID DBS to Enhance Access to testing

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Early Infant Diagnosis Through DBS Collection

Training remains a critical component to expanding access to EID

UNAIDS Joint Statement:

Recently issued by global partners reinforced the commitment to urgently address the challenges to the early diagnosis and treatment of children living with HIV, which led to **estimated death of 95,000 children in 2019**[1].

Coalition of governments and global partners have, in accordance with WHO guidelines, effectively implemented EID across multiple settings, with **training and capacity building of healthcare workers** on DBS Collection across PMTCT sites a key intervention.

Critical success factors to ensuring accurate, timely early diagnosis include the following: i) **obtaining high quality samples**, ii) **careful handling of specimens**; and iii) **maintaining accurate records**.

CLINTON HEALTH ACCESS INITIATIVE

Elizabeth Glaser Pediatric AIDS Foundation
Fighting for an AIDS-free generation

unicef

World Health Organization

[1] UNAIDS. Joint statement calling for urgent country scale-up of access to optimal HIV treatment for infants and children living with HIV. 22 December 2020

ASLM Resource Centre

Training material to enable critical successful factors for EID

ASLM Resource Centre Page

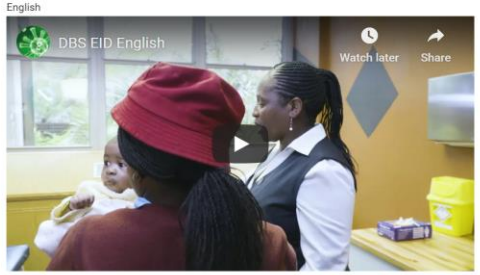
Early Infant Diagnosis Through Dried Blood Spot Collection

June 17, 2019

Facebook Twitter LinkedIn

Early infant diagnosis (EID) is critical for timely initiation of antiretroviral treatment (ART) in HIV-infected children who are at high risk of mortality. In recognition of the immense benefits of dried blood spot (DBS) as a means of increasing the access to EID, the World Health Organization, African Society for Laboratory Medicine, Centers for Disease Control and Prevention, United States Agency for International Development, Clinton Health Access Initiative, Médecins Sans Frontières, Global Fund, Riders for Health, Clinical Laboratory Standards Institute convened, identified and developed tools that would assist programs in scaling up HIV Diagnosis and uptake of results. This video, produced by the US Centers for Disease Control and Prevention English, French, and Portuguese, describes the procedure for collection of a DBS specimen from an infant below 18 months of age for performing HIV-1 PCR.

English



- In collaboration with global partners, CDC has led the development of training videos covering **EID through DBS collection.**
- In addition to explaining how to troubleshoot common issues, the videos outline how to:
  - *i) gather DBS supplies for EID*
  - *ii) collect DBS samples*
  - *iii) tell the difference between valid and invalid DBS; and*
  - *iv) ensure DBS cards are properly labelled and logged.*
- A pre- and post-test is available to help track progress
- In English , French and Portuguese, the videos can be accessed via ASLM's Resources Centre and YouTube.[1,2]

[1] ASLM. https://aslm.org/resource/early-infant-diagnosis-through-dried-blood-spot-collection/. 17 June 2019

[2] ASLM. https://www.youtube.com/watch?v=2FUlphI5PoU. 10 May 2018

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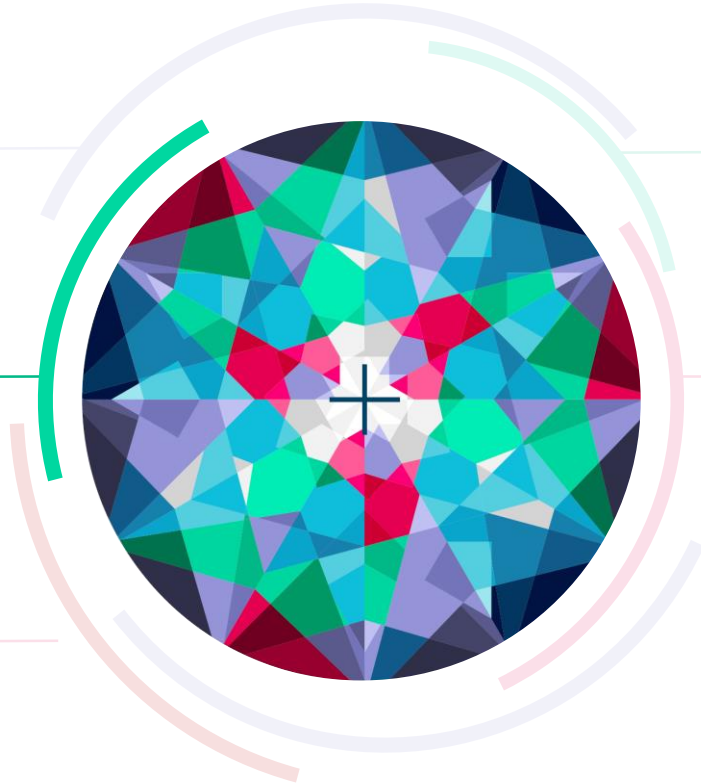
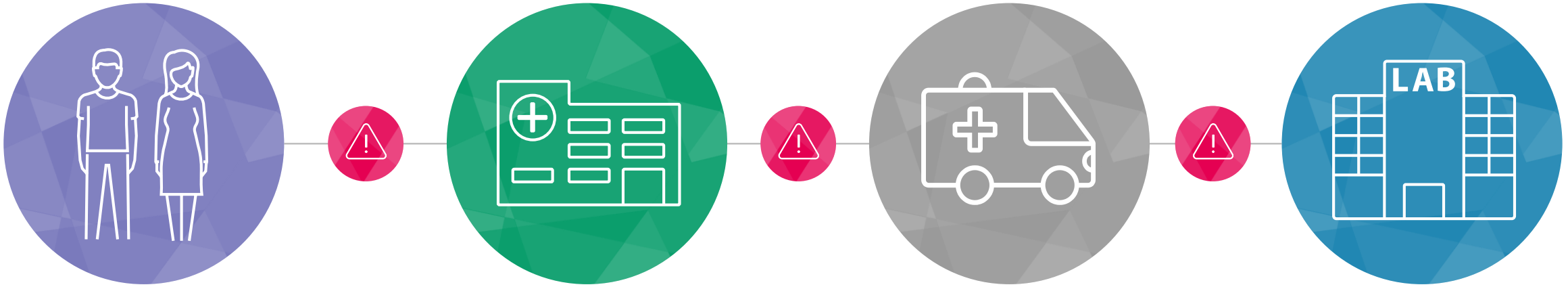


Limitations to Meeting Virally Suppressed Target – 95% by 2025

Barriers to plasma-quality Viral Load for patients across all settings

Not all people live close to a major health clinic

Infrastructure not in place to allow for optimal storage and transportation of EDTA Plasma Specimens i.e. cold chain



Those living in rural settings have blood taken in small clinics – centrifuge required for sample handling

DBS is an alternative sample type but a more effective solution is required

Use of DBS Can Cause Misclassification

Ideal for EID but not VL

Data from Vietnam shows 6% of patients misclassified using DBS

Downward misclassification

Believe patients failing treatment **are suppressed**

This could lead to **additional health complications** and the risk of infecting more people which both add to cost

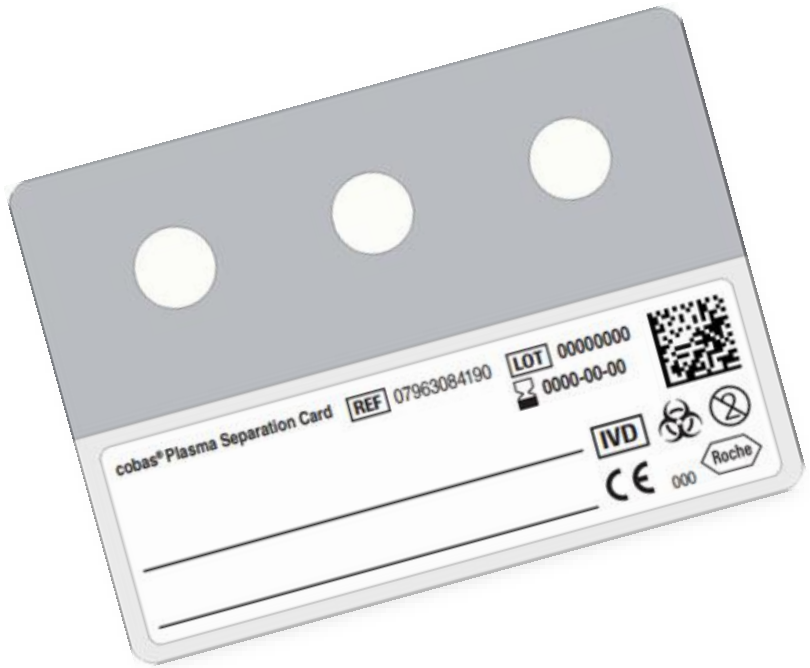
Upward misclassification

Believe suppressed patient is **failing treatment**

This leads to **additional costs** associated with adherence counselling and the change to more costly second line therapy

cobas® Plasma Separation Card

An effective alternative to DBS…



WHO standard of <1000 cp/mL (in plasma)
No other CE-marked or WHO prequalified sample collection solution matches performance

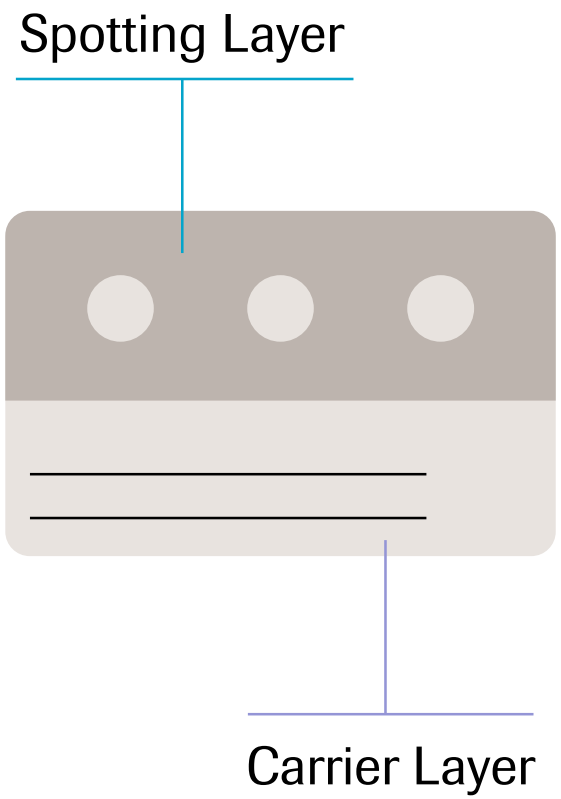
Superior solution compared to DBS
Better performance than DBS with low misclassification rates

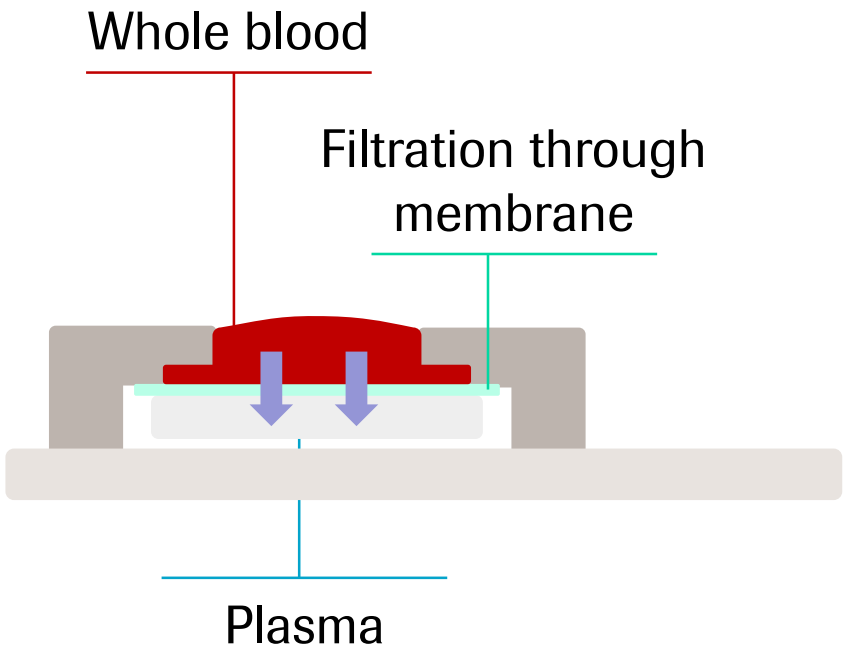
Easy handling, transport and storage
Provides an easy-to-use solution to monitor patients in remote areas

Plasma-based sample (gold standard)
Separates from whole blood
Stabilizes dried plasma/viral RNA under extreme heat and humidity

Correlation to plasma as the GOLD standard
Plasma is the preferred sample type for HIV viral load testing

Design of the cobas® Plasma Separation Card





Sample Collection Process for the cobas® Plasma Separation Card

1) Sample Collection

(140µL whole blood required per spot and one spot required)

Step 1 Remove primary packaging

Step 2 Prepare finger prick

Step 3 Collect blood

Step 4 Apply blood to spot

Step 5 Let card dry and package for shipment

2) Sample Transport from the Field to the Laboratory

(18-45ºC and up to 85% humidity (>21 days))

Step 1 Put dried card into sample bag

Step 2 Add desiccant

Step 3 Add cards to transport bag

Step 4 Ship transport bag to Centralized Laboratory

cobas® Plasma Separation Card Bundle Components

Convenient for clinics and patients, and simplifies ordering

Training and Support for cobas® Plasma Separation Card

*Tools to support implementation of **cobas**® PSC*

Roche has developed **training videos, posters and presentations** detailing how to use the **cobas**® Plasma Separation Card, specifically:

- Sample Collection Method
- Preparation for Sample Transportation
- Sample Preparation and Instrument Workflow for Roche systems (including **cobas**® 6800/8800 Systems, **cobas**® 4800 System and COBAS® AmpliPrep/COBAS® TaqMan® System)

Training material is available in English , French and Portuguese, and can be accessed via **ASLM's Resources Centre**

Mozambique Study

*Performance - Very low misclassification rates with **cobas**® PSC*

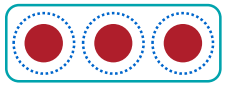
Misclassification rates of viral load values below 1000 c/ml

0.7%

Capillary specimen

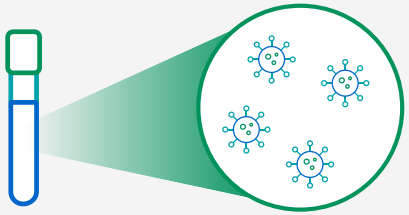
0.3%

Venous specimen



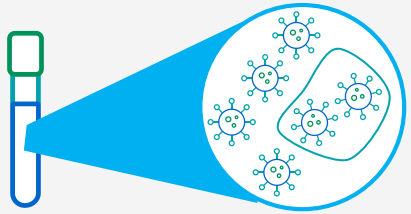
5.9%

DBS specimen



Eliminates the interference of cell-associated viral nucleic acid

No over-quantification



Cell-associated viral nucleic acid present in whole blood

Over-quantification

Vubil A, Zicai AF, Sitoe N, Nhachigule C, Meggi B, Loquiha O, et al. (2020) Accurate HIV viral load measurement in primary health care settings using the cobas® plasma separation card. PLoS ONE 15(5): e0232122. https://doi.org/ 10.1371/journal.pone.0232122

Milestones in regulatory process met

Evaluation Letter

- **Memorandum issued in 2019 by CDC** following evaluation study in South Africa

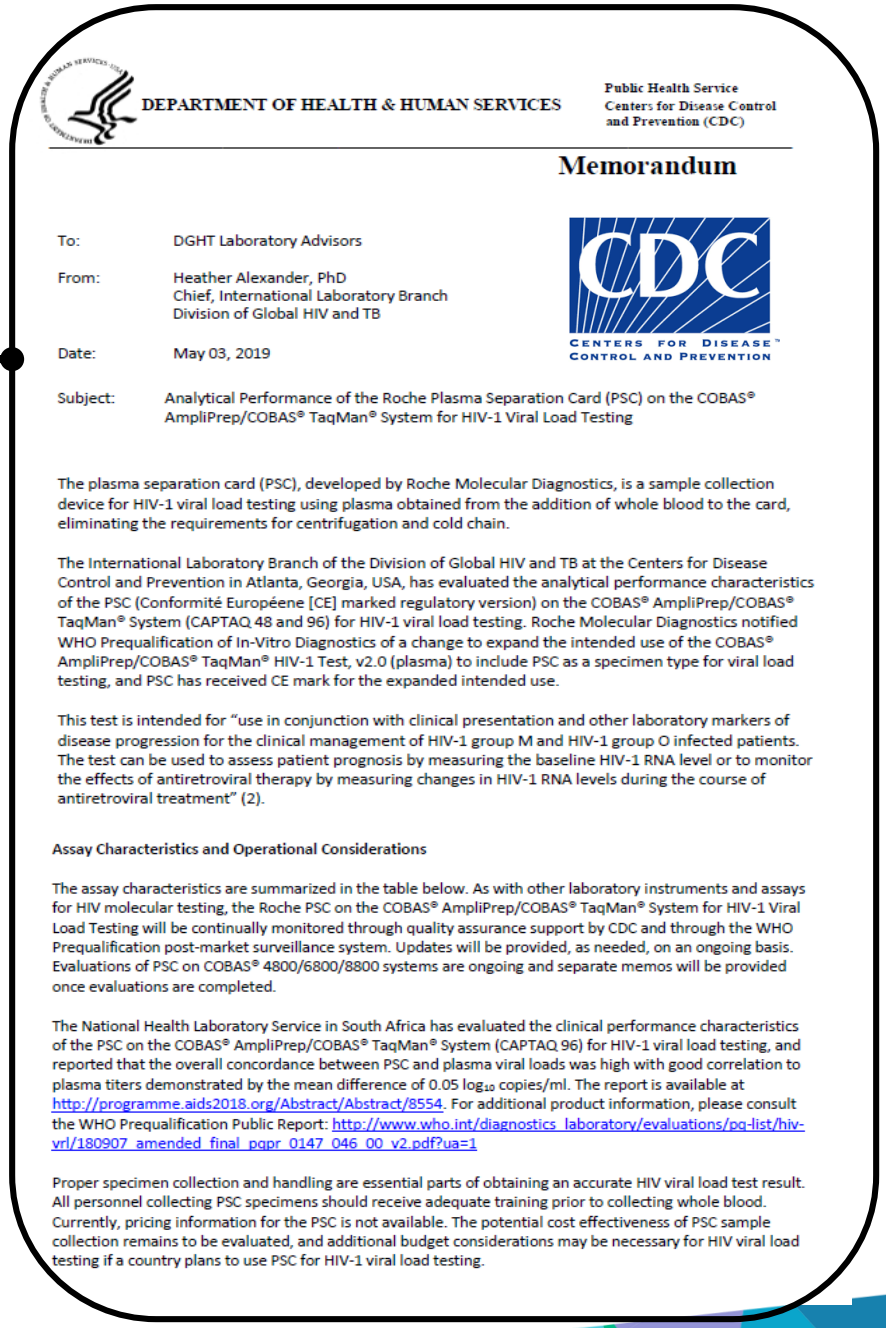
WHO Prequalification

- WHO Prequalified for **cobas® 6800/8800 Systems** and **COBAS® AmpliPrep/COBAS® TaqMan® System**, application submitted for **cobas® 4800 System**
- The **Limit of Detection estimated at 489 cp/mL** (95% CI: 330–1256) for cobas Plasma Separation Card (cobas® 6800/8800 Systems)

Verification Panels

- In partnership with **CDC development of verification panels (TBD)**

[1] WHO. WHO PQ of IVD - cobas HIV-1 Quantitative nucleic acid test for use on the cobas 6800/8800 Systems. October 2020



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Centers for Disease Control and Prevention (CDC)

Memorandum

To: DGHT Laboratory Advisors

From: Heather Alexander, PhD
Chief, International Laboratory Branch
Division of Global HIV and TB

Date: May 03, 2019

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Subject: Analytical Performance of the Roche Plasma Separation Card (PSC) on the COBAS® AmpliPrep/COBAS® TaqMan® System for HIV-1 Viral Load Testing

The plasma separation card (PSC), developed by Roche Molecular Diagnostics, is a sample collection device for HIV-1 viral load testing using plasma obtained from the addition of whole blood to the card, eliminating the requirements for centrifugation and cold chain.

The International Laboratory Branch of the Division of Global HIV and TB at the Centers for Disease Control and Prevention in Atlanta, Georgia, USA, has evaluated the analytical performance characteristics of the PSC (Conformité Européene [CE] marked regulatory version) on the COBAS® AmpliPrep/COBAS® TaqMan® System (CAPTAQ 48 and 96) for HIV-1 viral load testing. Roche Molecular Diagnostics notified WHO Prequalification of In-Vitro Diagnostics of a change to expand the intended use of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test, v2.0 (plasma) to include PSC as a specimen type for viral load testing, and PSC has received CE mark for the expanded intended use.

This test is intended for "use in conjunction with clinical presentation and other laboratory markers of disease progression for the clinical management of HIV-1 group M and HIV-1 group O infected patients. The test can be used to assess patient prognosis by measuring the baseline HIV-1 RNA level or to monitor the effects of antiretroviral therapy by measuring changes in HIV-1 RNA levels during the course of antiretroviral treatment" (2).

Assay Characteristics and Operational Considerations

The assay characteristics are summarized in the table below. As with other laboratory instruments and assays for HIV molecular testing, the Roche PSC on the COBAS® AmpliPrep/COBAS® TaqMan® System for HIV-1 Viral Load Testing will be continually monitored through quality assurance support by CDC and through the WHO Prequalification post-market surveillance system. Updates will be provided, as needed, on an ongoing basis. Evaluations of PSC on COBAS® 4800/6800/8800 systems are ongoing and separate memos will be provided once evaluations are completed.

The National Health Laboratory Service in South Africa has evaluated the clinical performance characteristics of the PSC on the COBAS® AmpliPrep/COBAS® TaqMan® System (CAPTAQ 96) for HIV-1 viral load testing, and reported that the overall concordance between PSC and plasma viral loads was high with good correlation to plasma titers demonstrated by the mean difference of 0.05 $\log_{10}$ copies/ml. The report is available at http://programme.aids2018.org/Abstract/Abstract/8554. For additional product information, please consult the WHO Prequalification Public Report: http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-vrl/180907_amended_final_pqpr_0147_046_00_v2.pdf?ua=1

Proper specimen collection and handling are essential parts of obtaining an accurate HIV viral load test result. All personnel collecting PSC specimens should receive adequate training prior to collecting whole blood. Currently, pricing information for the PSC is not available. The potential cost effectiveness of PSC sample collection remains to be evaluated, and additional budget considerations may be necessary for HIV viral load testing if a country plans to use PSC for HIV-1 viral load testing.

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**Streamlining
Verification of Assays**

Roche Assay Implementation Tool

Streamlining the verification of new assays for laboratories

Planning assistance for assay verification experiments for PCR based testing for CE-IVD or FDA approved assays*

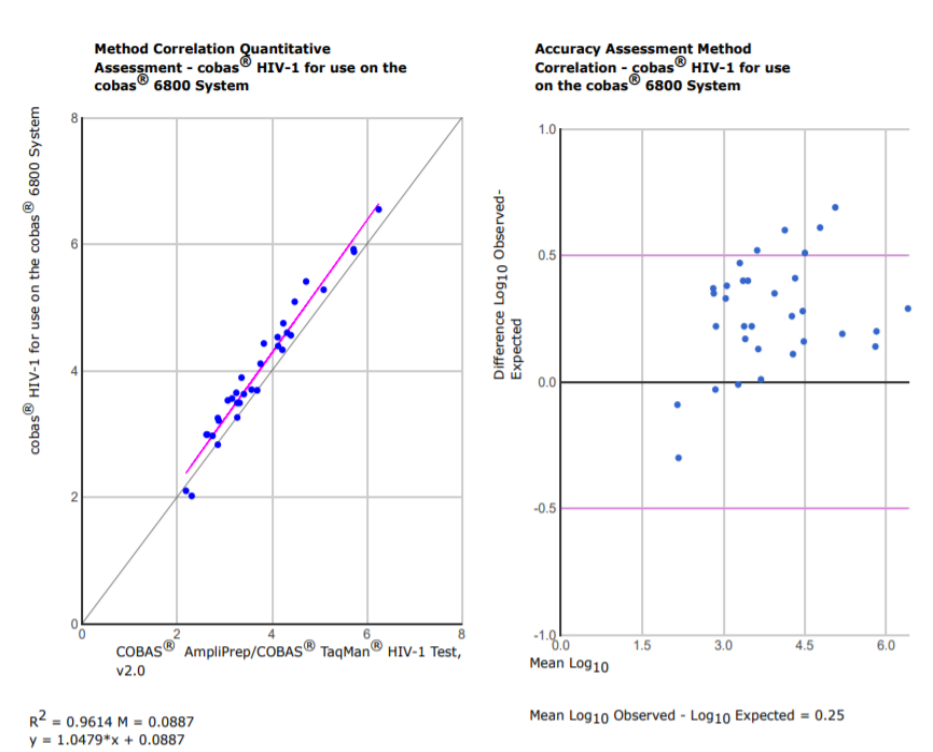
Data analysis of the performance specifications required for assay verification through a web-based portal

Report generation of analyzed data for assessment by authorized laboratory personal for verification sign-off and compliance requirements

**Tool in current format was developed for Roche PCR based IVD assays*

Roche Assay Implementation Tool

A support tool for laboratories across Africa for verification of IVDs



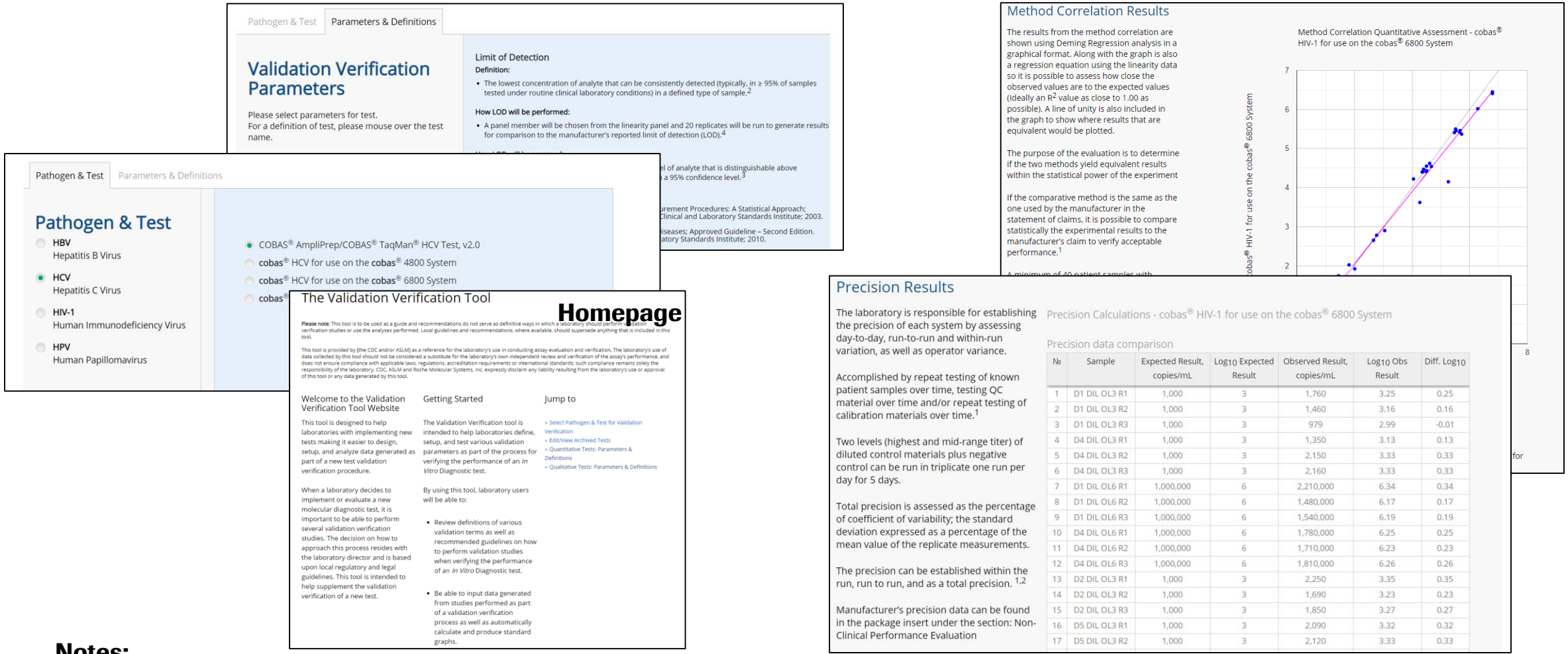
With the Assay Implementation Tool* labs will be able to:

- **Review** definitions of various verification terms as well as recommended guidelines **on how to perform studies** when verifying the performance of an *In Vitro* Diagnostic test
- **Input data** generated from studies performed as part of a verification process as well as **automatically calculate and produce standard graphs**
- **Document** (via .pdf format) for the laboratory's records the runs were performed as part of a verification study, including the results, data analyses generated, as well as other details associated

** Roche has worked in collaboration with CDC ILB team to modify the tool to meet verification parameters required per CDC guidelines.*

Roche Assay Implementation Tool

Accessible, easy to navigate, simple data input interface and report generation



Notes:

- Training video on using the tool (which will provide a technical overview) will be issued in parallel to the tool's release

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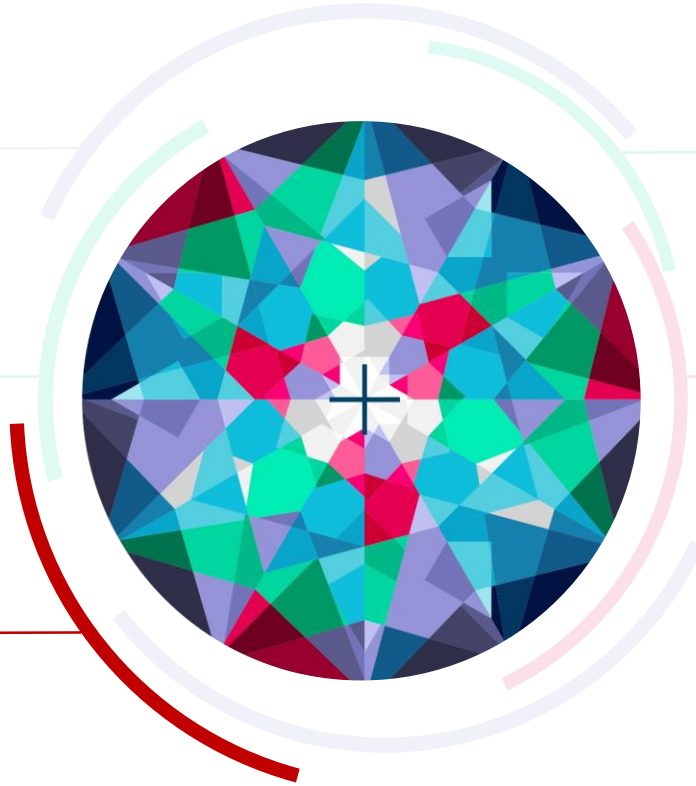

Summary & Questions

Tools to support capacity development and improve efficiencies in laboratory operations

Capacity building training materials available on ASLM Resource Center

- **DBS collection for EID testing**
- **cobas® Plasma Separation Card** (dried plasma spots), sample collection, transport and laboratory process and country implementation

Introducing a tool currently in development to help optimize laboratory operations *(timing for release to be determined)*

- Online, intuitive **Roche Assay Implementation Tool** to streamline planning and implementation of the verification process

Thank you to the contributors

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References

a	Shrivastava R et al. (2019)	Role of public-private partnerships in achieving UNAIDS HIV treatment targets	BMC Health Services Research
b	Roche and the US President's Emergency Plan for AIDS Relief (PEPFAR) partner to strengthen laboratories medicine training and knowledge on the African continent	From https://www.roche.com/media/releases/med-cor-2012-12-04.htm Accessed 5 Sept 2018	Roche
c	Joint statement calling for urgent country scale-up of access to optimal HIV treatment for infants and children living with HIV	From https://www.who.int/news/item/22-12-2020-joint-statement-calling-for-urgent-country-scale-up-of-access-to-optimal-hiv-treatment-for-infants-and-children-living-with-hiv Accessed 22 December 2020	WHO
d	Vubil A et al. (2020)	Accurate HIV viral load measurement in primary health care settings using the cobas® plasma separation card.	PLoS ONE 15(5): e0232122.
e	WHO PQ of IVD - cobas HIV-1 Quantitative nucleic acid test for use on the cobas 6800/8800 Systems	https://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-vrl/201026_amended_pqpr_0365_118_00_cobas_. Accessed October 2020	WHO

Doing now what patients need next

