TMDA/DMD/MDA/F/014
Rev #:00

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

PUBLIC ASSESSMENT REPORT FOR XPERT HIV-1 VL XC (RAPID VIRAL LOAD TESTING KIT)

Version number 2.0, 18.05.2026

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1. Introduction

XPERT HIV-1 VL XC is a class C in-vitro diagnostic device belonging to the immunology specialty category. It is approved in Tanzania as a single device for use in adults, children, elderly by healthcare professionals.

1.1. Administrative Information

Registration number	TAN 24 MDR 0074
Brand Name (if relevant)	XPERT HIV-1 VL XC
Common name	RAPID VIRAL LOAD TESTING KIT
Class of the device and rule applied	Class D as per Rule 1 for classification of In Vitro Diagnostic Devices
GMDN code and term	65101, HIV-1 nucleic acid IVD, kit, nucleic acid amplification technology (NAT)
Name and complete address of the Market Authorization Holder	Cepheid AB, Röntgenvägen 5, 171 54 Solna, Sweden
Name and address(es) of local responsible person (LRP).	KAS MEDICS Units UF09 & UF10, Umoja Complex Plot No. 11Nyerere Road, Vingunguti Industrial Area, P. O. Box 12019, Dar es salaam, Tanzania. Tel; +255 22 2861737/8 Email; kasregulatory@artemislife.com

1.2. Assessment Procedure

The application for registration of XPERT HIV-1 VL XC was submitted on 08.02.2023. The product underwent full assessment. Assessment was completed in 03 rounds of evaluation XPERT HIV-1 VL XC was registered on 29.05.2024.

2. Technical information

2.1. Intended use

The intended use of XPERT HIV-1 VL XC as declared by the manufacturer and approved by TMDA is quantification of human immunodeficiency virus type 1 (HIV-1) RNA in human EDTA plasma using the automated GeneXpert® System. XPERT HIV-1 VL XC is approved for use in healthcare settings by trained laboratory professionals only.

2.2. Device details and features

XPERT HIV-1 VL XC is a single device with accessories. XPERT HIV-1 VL XC has been registered as a kit which consists of Bead 1, Bead 2, and Bead 3 (freeze-dried) 1 of each per cartridge Lysis Reagent (Guanidinium Thiocyanate) 2.0 mL per cartridge Rinse Reagent 0.5 mL per cartridge Elution Reagent 1.5 mL per cartridge Binding Reagent 2.4 mL per cartridge Proteinase K Reagent 0.48 mL per cartridge Disposable 1 mL Transfer Pipettes 10 per kit CD 1 per kit Assay Definition File (ADF) Instructions to import ADF into GeneXpert software Instructions for Use (Package Insert) components. It is a closed system.

XPERT HIV-1 VL XC is a semi-automated device. It is used for monitoring of HIV-1. XPERT HIV-1 VL XC operates by reverse transcription polymerase chain reaction (RTPCR). The test out-put is quantitative.

The type of specimen used is blood plasma and is collected by venous blood.

GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequence in simple or complex samples using real-time RT-PCR. The systems consist of an instrument, personal computer, and preloaded software for running tests and viewing the results. The systems require.
single-use disposable GeneXpert cartridges that contain the RT-PCR reagents and carry out the sample extraction and RTPCR processes. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, refer to the appropriate GeneXpert Dx Operator Manual or GeneXpert Infinity Operator Manual. The HIV-1 VL XC test includes reagents for the detection of HIV-1 RNA in samples and two internal controls used for quantitation of HIV-1 RNA. The internal controls are also used to monitor the presence of inhibitor(s) in the RT and PCR reactions. Amplification and detection of HIV-1 RNA is achieved by primers and probes targeted to the highly conserved LTR region and the polymerase gene (dual target) of the HIV-1 genome. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

2.3. Commercial presentation

There are one approved commercial presentation as follows: (one) 1 test in the primary pouch. 10 number of test units in are placed in secondary carton box.

Additional contents include Bead 1, Bead 2, and Bead 3 (freeze-dried) 1 of each per cartridge Lysis Reagent (Guanidinium Thiocyanate) 2.0 mL per cartridge Rinse Reagent 0.5 mL per cartridge Elution Reagent 1.5 mL per cartridge Binding Reagent 2.4 mL per cartridge Proteinase K Reagent 0.48 mL per cartridge Disposable 1 mL Transfer Pipettes

10 per kit CD 1 per kit Assay Definition File (ADF) Instructions to import ADF into GeneXpert software Instructions for Use (Package Insert) components

2.4. Items required but not submitted

● GeneXpert Dx System or GeneXpert Infinity System (catalog number varies by configuration): GeneXpert instrument, computer with proprietary GeneXpert Software Version 4.7b or higher (GeneXpert Dx System), Xpertise™ 6.4b or higher (Infinity System), barcode scanner, and appropriate GeneXpert System operator manual
● Printer: If a printer is needed, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.
● Bleach or sodium hypochlorite
● Ethanol or denatured ethanol.

3. Storage instructions

3.1.1. Shelf-life

18 months.

3.1.2. Storage conditions

The recommended storage conditions are 2–28 °C.

3.1.3. Shipping conditions

The recommended shipping conditions is 2-28°C.

4. Manufacturing site audit

The manufacturer of the device is Cepheid AB, Röntgenvägen 5, 171 54 Solna, Sweden.

Quality audit of the manufacturing facility was conducted through site visit on 27th-28th December 2025. The site was found to be compliant to ISO 13485 requirements.

5. Performance Evaluation

5.1. Analytical Performance

The analytical performance characteristics of the device was established through the following test parameters: accuracy, trueness and precision.

5.2. Clinical Performance

Clinical performance was conducted at three different centers (Universita degli studi di Roma, Italy, MIB Dienstleistung GmbH, Germany, and University of the Free State, Republic of South Africa). The following parameters were tested; accuracy and precision.

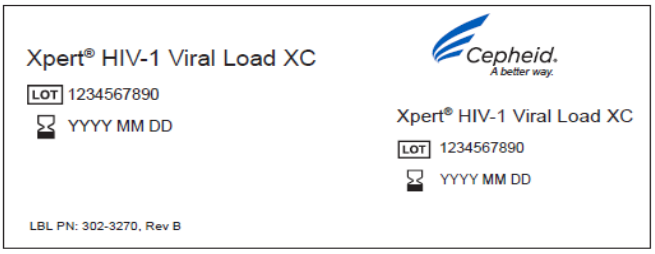
6. Product label and instructions for use

The content of the primary and secondary labels is in line with TMDA labeling requirements in terms of content, layout and design. The label contains sufficient information for proper identification of the device and post marketing follow up of the product in the market.

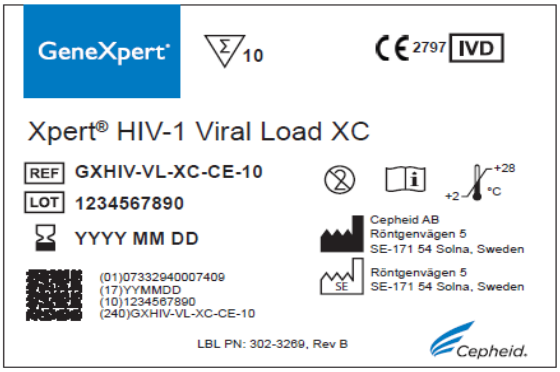
The user manual, package insert and instructions for use includes all the relevant information to ensure correct and safe use of the device by intended user.

6.1. Primary pack

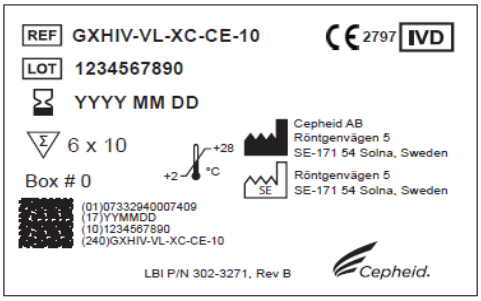
Cartridge
Stock Label p/n 300-5505, (latest rev)
Imprint Label p/n 302-3272, Rev A



Carton Side-Panel
Stock Label p/n 301-2307, (latest revision)
Imprint Label p/n 302-3270, Rev B



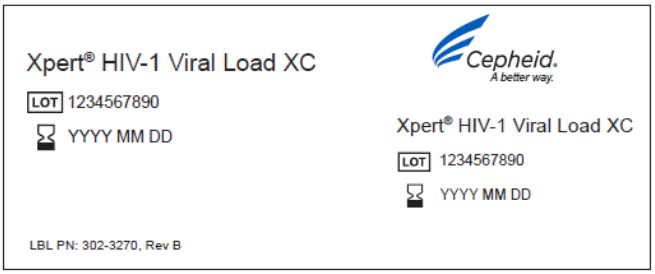
Kit 10-Cartridge Carton Top
Stock Label p/n 300-5445, (latest revision)
Imprint Label p/n 302-3269, Rev B



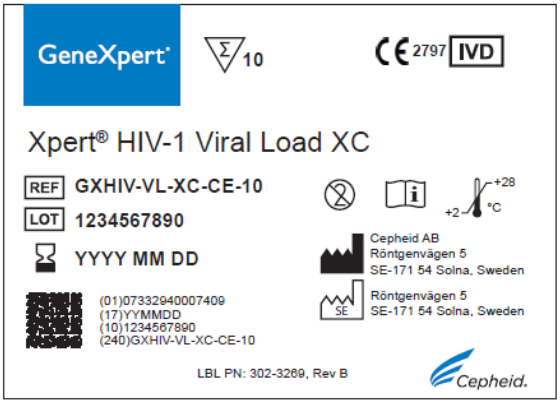
Outer Box
Stock Label p/n 301-7666, (latest revision)
Imprint Label p/n 302-3271, Rev B

6.2. Secondary pack

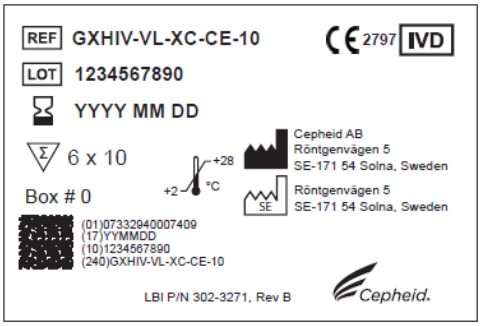
Cartridge
Stock Label p/n 300-5505, (latest rev)
Imprint Label p/n 302-3272, Rev A



Carton Side-Panel
Stock Label p/n 301-2307, (latest revision)
Imprint Label p/n 302-3270, Rev B



Kit 10-Cartridge Carton Top
Stock Label p/n 300-5445, (latest revision)
Imprint Label p/n 302-3269, Rev B



Outer Box
Stock Label p/n 301-7666, (latest revision)
Imprint Label p/n 302-3271, Rev B

6.3 Instructions for use/Package insert
Double Click here for instructions for use

Attachment 9 -
302-4124 Xpert HIV-1

7. Risk – Benefit Analysis

On basis of the data submitted, the current state of knowledge and compliance of the manufacturer to ISO 13485, the benefit of the product outweighs the risks associated with its use when used in accordance to the manufacturer instruction. **XPERT HIV-1 VL XC** is recommended for registration.

8. Post-approval updates

8.1. Variation applications

Reference number	Date submitted	Change requested	Recommendation	Granting date
NA	NA	NA	NA	NA

8.2. Feedback from pharmacovigilance, post marketing surveillance and enforcement activities

Type of feedback	Impact	Response
No any recorded Adverse Event	NA	NA

8.3. Re-registration applications

NA

CHANGE HISTORY

Version number	**Date**	**Description of update**	**Section(s) Modified**	**Approval date**

GeneXpert®
Powered By CEPHEID INNOVATION

Xpert® HIV-1 Viral Load XC

REF **GXHIV-VL-XC-CE-10**

CE 2797 IVD

Cepheid®

In Vitro Diagnostic Medical Device

302-4124, Rev. B April 2021

Trademark, Patents, and Copyright Statements

Xpert® HIV-1 Viral Load XC

For in Vitro Diagnostic Use Only.

1 Proprietary Name

Xpert® HIV-1 Viral Load XC

2 Common or Usual Name

HIV-1 VL XC

3 Intended Use

Xpert® HIV-1 Viral Load XC (Extended Coverage) is an in vitro reverse transcription polymerase chain reaction (RT-PCR) test for the quantification of human immunodeficiency virus type 1 (HIV-1) RNA in human EDTA plasma using the automated GeneXpert® System.

It is intended for use as an aid in clinical management of patients infected with HIV-1.

Xpert® HIV-1 Viral Load XC is intended for use in conjunction with clinical presentation and other laboratory markers for disease prognosis and for use as an aid in assessing viral response to antiretroviral treatment as measured by changes in plasma HIV-1 RNA levels from HIV-1 infected individuals.

Xpert® HIV-1 Viral Load XC is intended to be performed by trained professional users or trained healthcare workers in a laboratory setting.

Xpert® HIV-1 Viral Load XC is not intended to be used as a donor screening test for HIV-1 infection.

4 Summary and Explanation

Human Immunodeficiency Virus (HIV) is the etiologic agent of Acquired Immunodeficiency Syndrome (AIDS). HIV can be transmitted through sexual contact, exposure to infected blood, body fluids, or blood products, prenatal infection of a fetus, or perinatal or postnatal infection of a newborn.

Untreated HIV-1 infection is characterized by high-level viral production and CD4 T-cell destruction, despite an often lengthy clinical latency, to significant net loss of CD4 T cells and AIDS.

HIV diagnostics continue to be important for managing the treatment and care of HIV infected patients. Measurement of blood plasma HIV-1 RNA viral load using nucleic acid-based molecular diagnostic assays has been established as standard of care for assessing HIV-positive patient prognosis and response to antiretroviral therapy. Assessment of viral load levels is a strong predictor of the rate of disease progression and, by itself or in combination with CD4 T-cell counts, has great prognostic value.[1,2]

The HIV-1 VL XC test uses real-time reverse transcription polymerase chain reaction (RT-PCR) technology to achieve high sensitivity for the quantitative detection of HIV-1 RNA in human plasma from HIV-1 infected individuals.

5 Principle of the Procedure

GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequence in simple or complex samples using real-time RT-PCR. The systems consist of an instrument, personal computer, and preloaded software for running tests and viewing the results. The systems require

single-use disposable GeneXpert cartridges that contain the RT-PCR reagents and carry out the sample extraction and RT-PCR processes. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, refer to the appropriate *GeneXpert Dx Operator Manual* or *GeneXpert Infinity Operator Manual*.

The HIV-1 VL XC test includes reagents for the detection of HIV-1 RNA in samples and two internal controls used for quantitation of HIV-1 RNA. The internal controls are also used to monitor the presence of inhibitor(s) in the RT and PCR reactions. Amplification and detection of HIV-1 RNA is achieved by primers and probes targeted to the highly conserved LTR region and the polymerase gene (dual target) of the HIV-1 genome. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The HIV-1 VL XC test is standardized against the 4th World Health Organisation (WHO) International Standard for HIV-1 (NIBSC code 16/194).[3]

6 Materials Provided

The HIV-1 VL XC kit contains sufficient reagents to process 10 samples. The kit contains the following:

HIV-1 VL XC Cartridges with Integrated Reaction Tubes	**10**
Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
Lysis Reagent (Guanidinium Thiocyanate)	2.0 mL per cartridge
Rinse Reagent	0.5 mL per cartridge
Elution Reagent	1.5 mL per cartridge
Binding Reagent	2.4 mL per cartridge
Proteinase K Reagent	0.48 mL per cartridge
Disposable 1 mL Transfer Pipettes	**10 per kit**
CD	**1 per kit**
Assay Definition File (ADF)	
Instructions to import ADF into GeneXpert software	
Instructions for Use (Package Insert)	

Note Safety Data Sheets (SDS) are available at www.cepheid.com or www.cepheidinternational.com under the **SUPPORT** tab.

Note The bovine serum albumin (BSA) in the beads within this product was produced and manufactured exclusively from bovine plasma sourced in the United States. No ruminant protein or other animal protein was fed to the animals; the animals passed ante- and post-mortem testing. During processing, there was no mixing of the material with other animal materials.

7 Storage and Handling

- Store the HIV-1 VL XC test cartridges at 2–28 °C.
- Prior to use, bring the HIV-1 VL XC test cartridges to 15–30 °C if they have been stored cold.
- Do not open the cartridge lid until you are ready to perform the test.
- Use cartridge within 4 hours after opening the cartridge lid and adding sample.
- Do not use a cartridge that has leaked.
- Do not use cartridges that previously have been frozen.
- Do not use a cartridge past the expiration date.

8 Materials Required but not Provided

- GeneXpert Dx System or GeneXpert Infinity System (catalog number varies by configuration): GeneXpert instrument, computer with proprietary GeneXpert Software Version 4.7b or higher (GeneXpert Dx System), Xpertise™ 6.4b or higher (Infinity System), barcode scanner, and appropriate GeneXpert System operator manual
- Printer: If a printer is needed, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.
- Bleach or sodium hypochlorite
- Ethanol or denatured ethanol

9 Warnings and Precautions

- For *in vitro* diagnostic use only.
- Treat all biological samples, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological samples should be treated with standard precautions. Guidelines for samples handling are available from the U.S. Centers for Disease Control and Prevention and the Clinical and Laboratory Standards Institute (CLSI).[4,5]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Appropriate safety measures should be taken in the event of a splash that may occur using bleach and facilities for adequate eye washing or skin rinsing are advised to care for such events.
- Biological samples, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution’s environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific disposal. If country or regional regulations do not provide clear direction on proper disposal, biological samples and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines.[6]
- Do not substitute HIV-1 VL XC test reagents with other reagents.
- Do not use a cartridge that has been dropped after removing it from the packaging.
- Do not shake the cartridge. Shaking or dropping the cartridge after opening the lid may yield invalid results.
- Do not place the sample ID label on the cartridge lid or on the barcode label.
- Each single-use HIV-1 VL XC test cartridge is used to process one sample. Do not reuse spent cartridges.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use disposable pipette is used to transfer one sample. Do not reuse spent disposable pipettes.
- If using a precision pipette: Each single use disposable pipette tip is used to transfer one sample. Do not reuse spent pipette tips.
- Wear clean lab coats and gloves. Change gloves between processing each sample.
- In the event of contamination of the work area or equipment with samples, thoroughly clean the contaminated area with a freshly prepared solution of 0.5% sodium hypochlorite (or a 1:10 dilution of household chlorine bleach). Follow by wiping the surface with 70% ethanol. Let the work surfaces dry completely before proceeding.
- For Instrument System cleaning and disinfecting instructions, refer to the appropriate *GeneXpert Dx System Operator Manual* or *GeneXpert Infinity System Operator Manual*.

10 Chemical Hazards[7,8]

Signal Word: WARNING

UN GHS Hazard Statements

- Harmful if swallowed.
- Causes mild skin irritation.
- Causes eye irritation.

UN GHS Precautionary Statements
Prevention

- Wash thoroughly after handling.

Response

- Call a POISON CENTER or doctor/physician if you feel unwell.
- If skin irritation occurs: Get medical advice/attention.
- IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
- If eye irritation persists: Get medical advice/attention.

11 Sample Collection, Transport, and Storage

Whole blood should be collected in BD Vacutainer® PPT™ Plasma Preparation Tubes for Molecular Diagnostic Test Methods, or in sterile collection tubes using K2 EDTA as the anticoagulant. Whole blood should be centrifuged to separate the plasma and red blood cells per the manufacturer's instructions.

- A minimum of 1 mL plasma is required for the HIV-1 VL XC test. If using the transfer pipette included in the kit, fill the transfer pipette with plasma to just below the bulb to transfer the required volume. Alternatively, if using a precision pipette, a minimum of 1 mL plasma is required. See Section 12.2 Preparing the Cartridge, step 6.
- Prior to plasma separation, whole blood collected in BD Vacutainer PPT Plasma Preparation Tubes for Molecular Diagnostic Test Methods, or in sterile collection tubes using K2 EDTA as the anticoagulant may be held at 2–30 °C for up to 24 hours.
- Plasma should be removed from the primary collection tube after centrifugation for storage. Plasma separated from whole blood may be held in secondary tubes at 2–35 °C for up to 24 hours, at 2–8 °C for up to 7 days or frozen (≤ -18 °C and ≤ -70 °C) for up to 6 weeks prior to testing.
- Plasma sample are stable for up to five freeze/thaw cycles. Thaw sample at 15–30 °C.
- Transportation of whole blood or plasma samples must comply with country, federal, state and local regulations for the transportation of etiologic agents.

12 Procedure

12.1 Preparing the Sample

1. Following centrifugation of whole blood samples, plasma may be pipetted directly into the test cartridge. Sufficient volume is critical to obtaining valid test results (see Section 12.2 Preparing the Cartridge).
2. Completely thaw and equilibrate frozen plasma samples to 15–30 °C prior to testing.
3. Remove plasma samples stored at 2–8 °C from the refrigerator and equilibrate to 15–30°C prior to testing.
4. Vortex plasma samples stored at 2–8 °C or frozen and thawed for 15 seconds before use.
5. If the plasma samples are cloudy, clarify by a quick (10 second) centrifugation before use.

12.2 Preparing the Cartridge

Important **Start the test within 4 hours of adding the sample to the cartridge.**

Note Pipetting no plasma or less than 1 mL of plasma into the cartridge will trigger an insufficient volume error (ERROR 2096 and ERROR 2097 respectively) preventing the instrument from running the sample.

1. Wear protective disposable gloves.
2. Allow HIV-1 VL XC test cartridges and sample to equilibrate to 15–30 °C prior to pipetting plasma into the cartridge.
   - Do not pipette plasma into a cartridge that is cold (below 15°C).
3. Inspect the test cartridge for damage. If damaged, do not use it.
4. Label the cartridge with sample identification.
5. Open the lid of the test cartridge.
6. Add the sample to the test cartridge.
   - If using the *transfer pipette* included in the kit (Figure 1), fill the pipette to just below the bulb to transfer at least 1 mL plasma from the tube (Figure 1). Make sure no large air bubbles are created in the pipette tip while filling the pipette. Empty the contents of the pipette into the sample chamber of the cartridge (Figure 2).

- If using a *precision pipette*, pre-wet the pipette tip once, by filling the pipette tip with plasma and emptying it into the tube. Then, using the pre-wet pipette tip, fill the pipette with at least 1 mL plasma from the tube. Empty the contents of the pipette into the sample chamber of the cartridge (Figure 2).

Note Do not remove the thin plastic film that covers the inner ring of the cartridge.

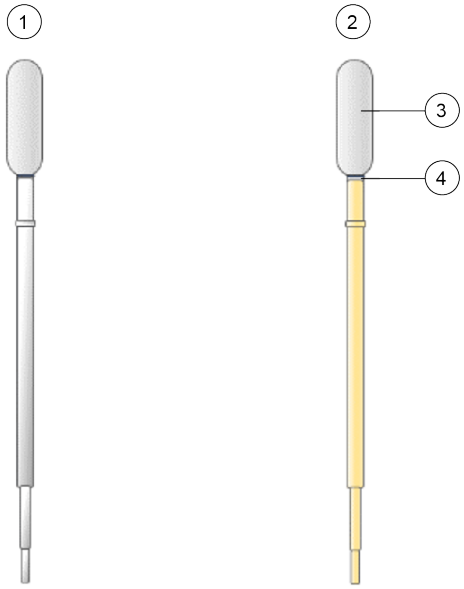


Figure 1. Transfer Pipette

Number	Description
1	Empty pipette
2	Filled pipette
3	Bulb
4	Fill plasma to just below the bulb.

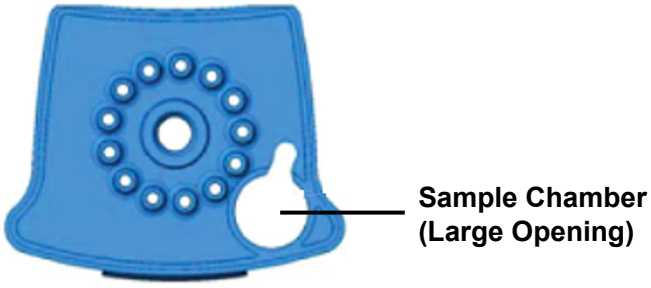


Figure 2. Cartridge (Top View)

7. Close the cartridge lid. Ensure the lid snaps firmly into place.

12.3 Starting the Test

Important **If you are running a *GeneXpert Dx system*, before you start the test, make sure that the system is running GeneXpert Dx software version 4.7b or higher and that the correct assay definition file is imported into the software.**

Important **If you are running a *GeneXpert Infinity system*, before you start the test, make sure that the system is running Xpertise software version 6.4b or higher and that the correct assay definition file is imported into the software.**

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*, depending on the model that is being used.

Note The steps you follow can be different if the system administrator changed the default workflow of the system.

1. Turn on the GeneXpert instrument:
   - If using the *GeneXpert Dx instrument*, first turn on the GeneXpert Dx instrument, and then turn on the computer. The GeneXpert software will launch automatically. If it does not, double-click the GeneXpert Dx software shortcut icon on the Windows® desktop.

     or
   - If using the *GeneXpert Infinity instrument*, power up the instrument. The Xpertise software will launch automatically. If it does not, double-click the Xpertise software shortcut icon on the Windows® desktop.
2. Log on to the GeneXpert Instrument System software using your username and password.
3. In the **GeneXpert System** window, click **Create Test** (GeneXpert Dx) or **Orders** and **Order Test** (Infinity). The **Create Test** window opens. The **Scan Patient ID barcode** dialog box opens.
4. Scan or type in the Patient ID. If typing the Patient ID, make sure the Patient ID is typed correctly. The Patient ID is associated with the test results and is shown in the **View Results** window and all the reports. The **Scan Sample ID barcode** dialog box opens.
5. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is associated with the test results and is shown in the **View Results** window and all the reports. The **Scan Cartridge Barcode** dialog box opens.
6. Scan the barcode on the cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.

Note If the barcode on the cartridge does not scan, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the software and the assay definition file is not available, a screen will appear indicating the assay definition file is not loaded on the system. If this screen appears, contact Cepheid Technical Support.

7. Click **Start Test** (GeneXpert Dx) or **Submit** (Infinity). In the dialog box that appears, type your password, if required.
8. For the *GeneXpert Infinity System*, place the cartridge on the conveyor belt. The cartridge will be automatically loaded, the test will run, and the used cartridge will be placed into the waste container.

   or

   For the *GeneXpert Dx Instrument*:

   a) Open the instrument module door with the blinking green light and load the cartridge.
   b) Close the door. The test starts and the green light stops blinking. When the test is finished, the light turns off.
   c) Wait until the system releases the door lock before opening the module door. Then remove the cartridge.
   d) Dispose of the used cartridges in the appropriate specimen waste containers according to your institution's standard practices.

13 Viewing and Printing Results

This section lists the basic steps for viewing and printing results. For more detailed instructions on how to view and print the results, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*, depending on the model being used.

Note If reporting results using a LIS, confirm that LIS results match system results for the patient ID field; if results conflict, report the system results only.

1. Click the **View Results** icon to view results.
2. Upon completion of the test, click the **Report** button of the **View Results** window to view and/or generate a PDF report file.

14 Quality Control

Each test includes a Sample Volume Adequacy (SVA) control, Internal Quantitative Standard High and Low (IQS-H and IQS-L), Lot Specific Parameters (LSP), and a Probe Check Control (PCC).

- **Sample Volume Adequacy (SVA)**: Ensures that the sample was correctly added to the cartridge. The SVA verifies that the correct volume of sample has been added in the sample chamber. The SVA passes if it meets the acceptance criteria. If the SVA does not pass, an `ERROR 2096` will display if there is no sample or an `ERROR 2097` if there is not enough sample. The system will prevent the test to be processed.
- **Internal Quantitative Standard High and Low (IQS-H and IQS-L)**: IQS-H and IQS-L are two Armored RNA® controls unrelated to HIV that are included in each cartridge and go through the whole test process. They are used for quantitation by using lot specific parameters for the calculation of HIV-1 RNA concentration in the sample. Additionally, IQS-H and IQS-L detect specimen-associated inhibition of the RT-PCR reaction, thereby acting as sample processing controls. The IQS-H and IQS-L pass if Cycle thresholds (Cts) are within valid range.
- **Lot Specific Parameters (LSP) for Quantitation** – Each kit lot has built-in LSP generated from an HIV-1 calibration panel, traceable to the 4th WHO International Standard for HIV-1 (NIBSC code 16/194), and the IQS-H and IQS-L. The LSP are unique for each kit lot and are used to ensure correct quantitation.
- **Probe Check Control (PCC)**: Before the start of the PCR reaction, the GeneXpert Instrument System measures the fluorescence signal from the probes to monitor bead rehydration, reaction tube filling, probe integrity, and dye stability. The PCC passes if the fluorescence signals meet the assigned acceptance criteria.

15 Interpretation of Results

The results are interpreted automatically by the GeneXpert Instrument System from measured fluorescent signals and embedded calculation algorithms and are clearly shown in the View Results window (Figure 3 and Figure 4). Possible results are shown in Table 1.

Table 1. Results and Interpretation

Result	Interpretation
HIV-1 DETECTED **XX copies/mL (log X.XX)** See Figure 3.	HIV-1 RNA is detected at XX copies/mL (log X.XX) ● HIV-1 RNA has quantitative value within the quantitative range of the test - (40-1x10^7 copies/mL). ● IQS-H and IQS-L: PASS. ● Probe Check: PASS; all probe check results pass.
HIV-1 DETECTED **> 1 × 10^7 copies/mL** See Figure 4.	HIV-1 RNA is detected above the analytical measurement range. ● IQS-H and IQS-L: PASS. ● Probe Check: PASS. All probe check results pass.
HIV-1 DETECTED **< 40 copies/mL** See Figure 5.	HIV-1 RNA is detected below the analytical measurement range. ● IQS-H and IQS-L: PASS. ● Probe Check: PASS. All probe check results pass.
HIV-1 NOT DETECTED See Figure 6.	HIV-1 RNA is not detected. This result does not infer that the patient has been cleared of the virus. ● IQS-H and IQS-L: PASS. ● Probe Check: PASS. All probe check results pass.
INVALID See Figure 7.	Presence or absence of HIV-1 RNA cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure. ● IQS-H and/or IQS-L: FAIL; Cycle thresholds (Cts) are not within valid range. ● Probe Check: PASS. All probe check results pass.

Result	Interpretation
ERROR See Figure 8.	Presence or absence of HIV-1 RNA cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure. • Probe Check: FAIL; all or one of the probe check results fail.
NO RESULT	Presence or absence of HIV-1 RNA cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure. A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress.

Note Results can be converted from copies/mL to IU/mL within the software. Please see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual* for instructions on how to change this setting.

The conversion factor for the HIV-1 VL XC test is 1 copy = 2.06 International Unit (IU).

Note Assay screenshots are for example only. The version number may vary from the screenshots shown in this package insert.

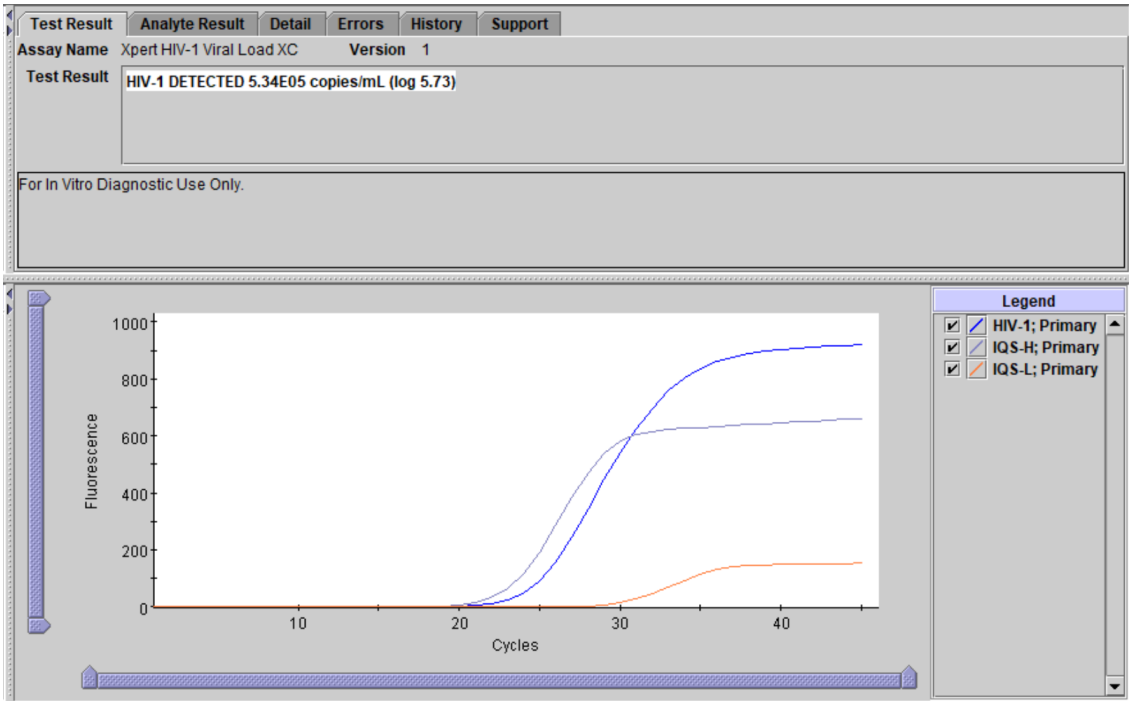


Figure 3. HIV-1 Detected and Quantified

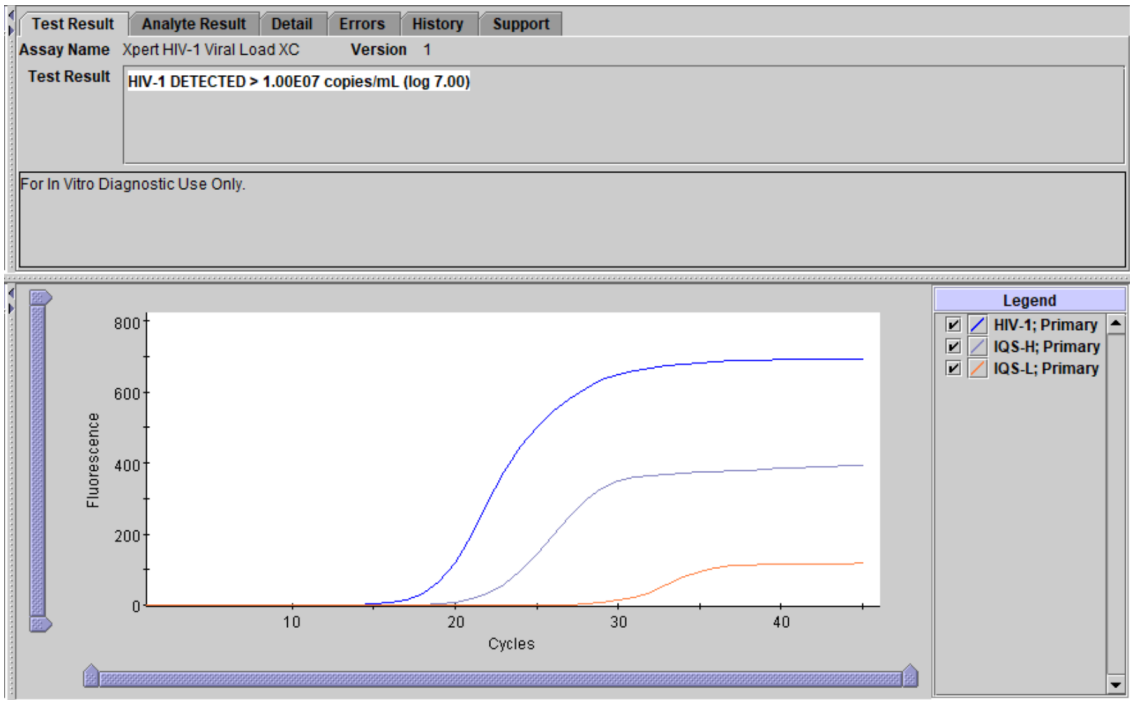


Figure 4. HIV-1 Detected but with titer above the quantitative range of the test

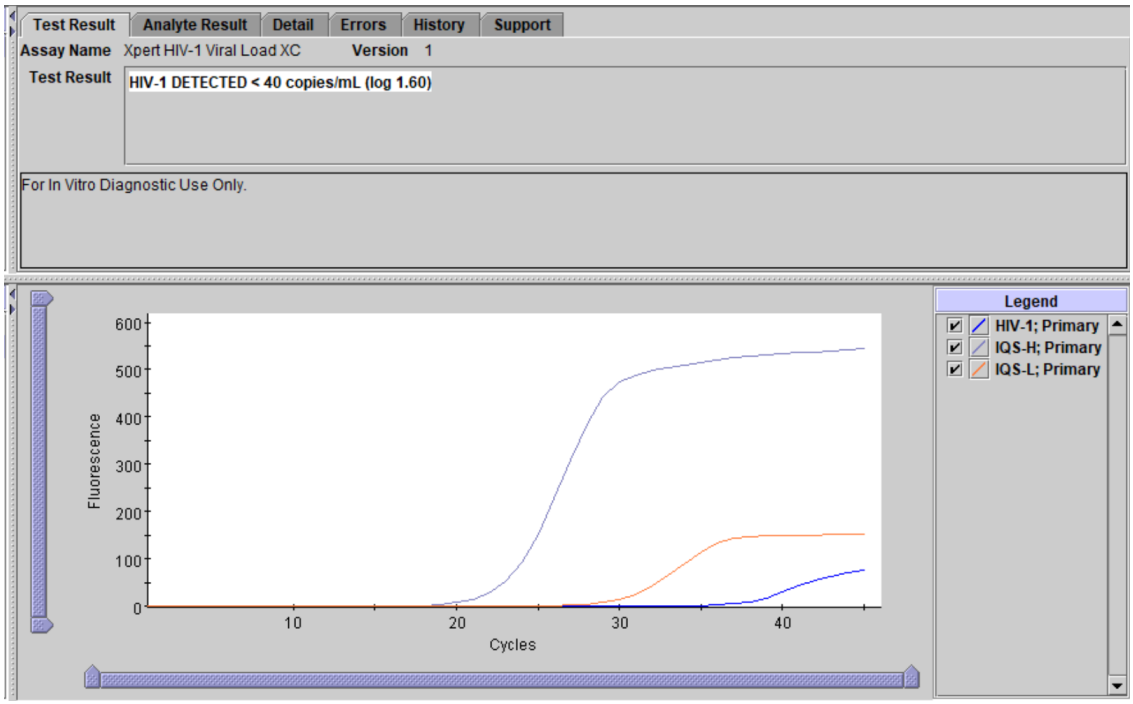


Figure 5. HIV-1 Detected but with titer below the quantitative range of the test

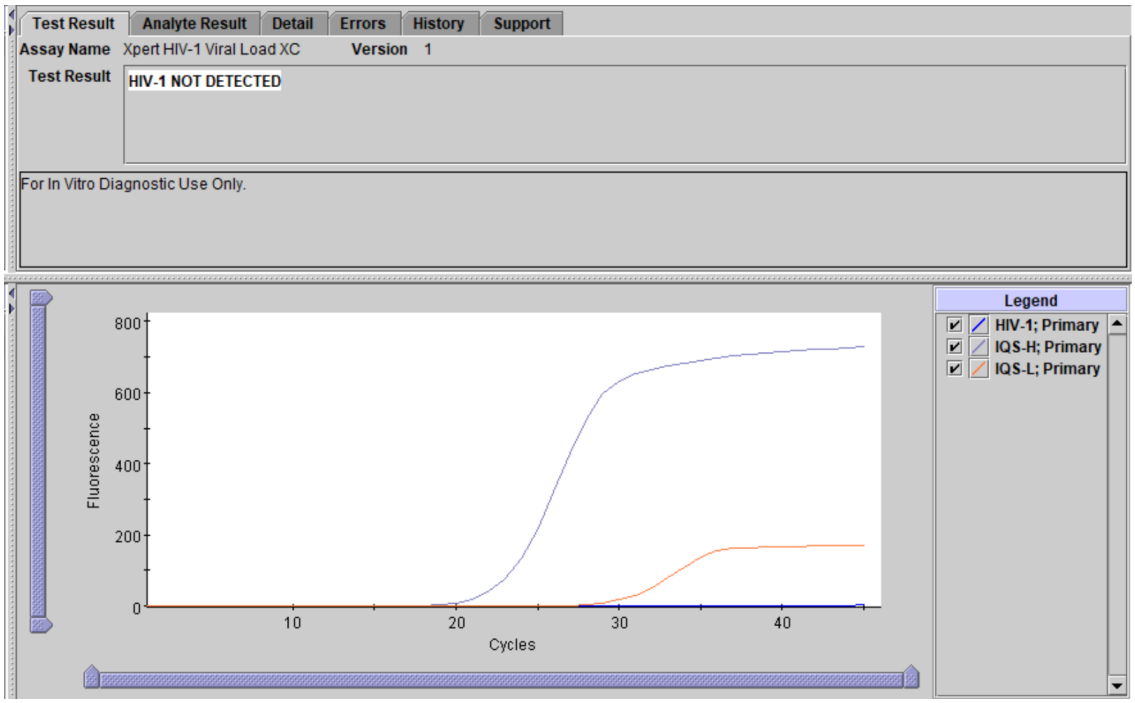


Figure 6. HIV-1 Not detected

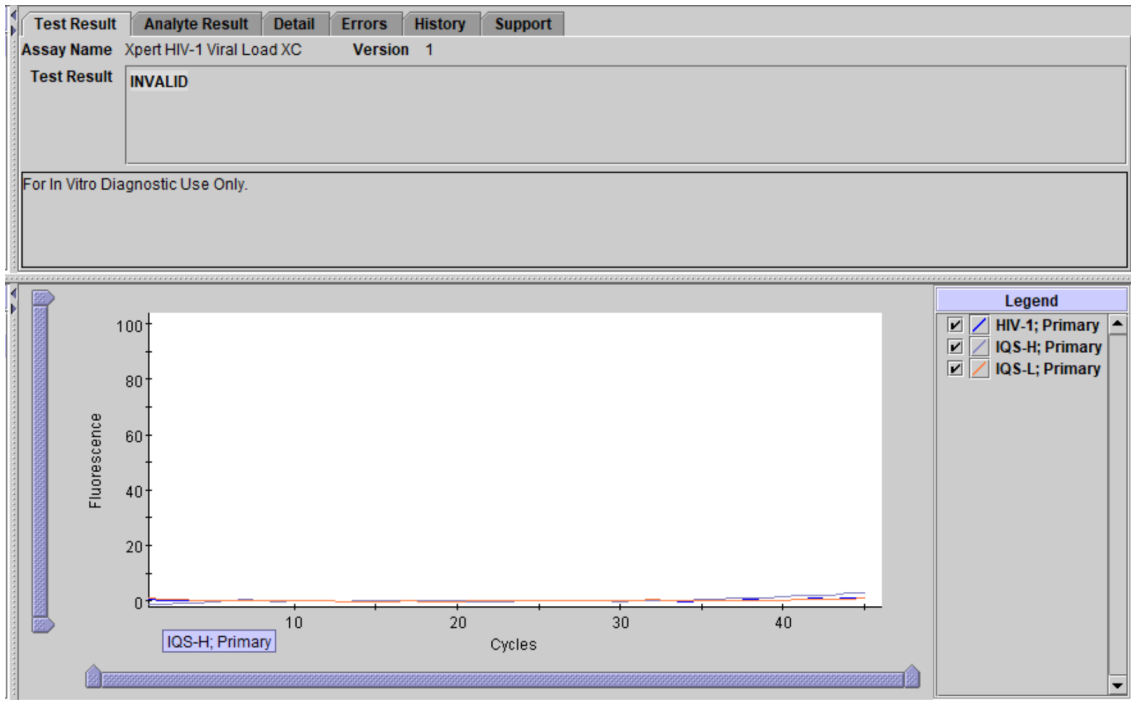


Figure 7. Invalid Result

Figure 8. Error

16 Retests

16.1 Reasons to Repeat the Test

If any of the test results mentioned below occur, repeat the test according to instructions in Section 16.2.

- An **INVALID** result indicates one or more of the following:
  - The IQS-H and/or IQS-L Cts are not within valid range.
  - The sample was not properly processed, or PCR was inhibited.
- An **ERROR** indicates that the test was aborted. Possible causes include: insufficient volume of sample was added, the reaction tube was filled improperly, a reagent probe integrity problem was detected, or the maximum pressure limit was exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress, or a power failure occurred.

16.2 Retest Procedure

If the result of a test is **INVALID**, **ERROR**, or **NO RESULT**, use a new cartridge to retest the affected sample (do not re-use the cartridge).

1. Remove a new cartridge from the kit.
2. Go to Section 12, Procedure, including Section 12.2, Preparing the Cartridge, and Section 12.3, Starting the Test.

17 Limitations

- Good laboratory practice and changing gloves between handling samples are recommended to avoid contamination of samples or reagents.
- Rare mutations, deletions or insertions within the target regions of the HIV-1 VL XC test may affect primer and/or probe binding resulting in under-quantitation or failure to detect the virus.

- The HIV-1 VL XC test has been validated only for use with K2 EDTA and PPT-EDTA plasma. Testing of other sample types may lead to inaccurate results.
- A negative test result does not preclude HIV-1 infection. Results from the HIV-1 VL XC test should be interpreted in conjunction with clinical presentation and other laboratory markers.
- Prior to switching from one technology to the next, Cepheid recommends that users perform method correlation studies in their laboratory to qualify technology differences.
- Reliable results are dependent on adequate sample collection, transport, storage and processing.
- Quantitation of HIV-1 RNA is dependent on the number of virus particles present in a sample and may be affected by sample collection methods, patient factors (i.e., age, presence of symptoms), and/or stage of infection.
- A sample that yields an **INVALID** result twice may contain an inhibitor; retesting is not recommended.

18 Performance Characteristics

18.1 Limit of Detection

The limit of detection (LoD) of the HIV-1 VL XC test was determined for group M subtype B by testing serial dilutions prepared from the WHO 4th International Standard for HIV-1 (NIBSC code: 16/194) in HIV-1 negative K2 EDTA plasma. In total six different concentration levels of the WHO International Standard and one negative were tested with three kit lots. Each concentration level was tested across three days with 24 replicates per kit lot for a total of 72 replicates per concentration level.

The results are shown in Table 2. The study demonstrated that the HIV-1 VL XC test detected HIV-1 RNA for the WHO International Standard at a concentration of 13.6 copies/mL in K2 EDTA plasma with a positivity rate of 95% as determined by PROBIT regression.

Table 2. Limit of Detection for the HIV-1 VL XC test using the 4th WHO International Standard for HIV-1

Group/Subtype	Nominal HIV-1 Concentration (copies/mL)	Number of Valid Replicates	Number of Positive Replicates	Positivity Rate (%)	LoD with 95% Probability Estimated by Probit (95% Confidence Interval)
Group M/ Subtype B	0	72	0	0	13.6 copies/ mL (11.7-15.6)
	1	72	13	18	
	2.5	72	31	43	
	5	72	45	63	
	10	72	60	83	
	20	72	70	97	
	40	72	72	100	

The limit of detection for the HIV-1 group M subtypes A, C, D, F, G, H, J, K, CRF-A/B, CRF-A/E, CRF-A/G, CRF-B/C, CRF-06, group N, group O and group P was determined by testing serial dilutions of cell culture stocks or clinical specimens representing each HIV-1 group and subtype in HIV-1 negative K2 EDTA plasma. In total six concentration levels of each HIV-1 group and subtype was tested with one kit lot across three days for a total of 24 replicates per concentration level.

The assignment of the nominal concentration of the cell culture stocks and clinical specimens was determined using CE-marked HIV-1 viral load tests.

The HIV-1 RNA concentration that can be detected with a positivity rate of 95% was determined by PROBIT regression. The results for each HIV-1 group M subtypes A, C, D, F, G, H, J, K, CRF-A/B, CRF-A/E, CRF-A/G, CRF-B/C, CRF-06, group N, group O and group P are shown in Table 3.

Table 3. Limit of Detection for HIV-1 group M subtypes A, C, D, F, G, H, J, K, CRF-A/B, CRF-A/E, CRF-A/G, CRF-B/C, CRF-06, group N, group O and group P in K2 EDTA Plasma

Group	Subtype	LoD by PROBIT (copies/mL)	95% Confidence Interval (copies/mL)
Group M	A	15.9	12.1-19.7
	C	13.2	10.2-16.3
	D	17.7	13.5-21.8
	F	18.1	14.5-21.6
	G	18.0	13.7-22.3
	H	7.9	6.2-9.5
	J	14.2	10.6-17.7
	K	16.9	12.7-21.0
	CRF A/B	13.1	9.9-16.3
	CRF A/E	14.2	10.7-17.6
	CRF A/G	17.4	13.2-21.6
	CRF B/C	17.0	13.3-20.8
	CRF 06	10.8	8.4-13.2
Group N	N/A	16.5	12.2-20.8
Group O	N/A	9.0	6.8-11.1
Group P	N/A	4.9	3.9-5.9

18.2 Lower Limit of Quantification

The lower limit of quantitation (LLoQ) is defined as the lowest concentration of HIV-1 RNA that is quantified with acceptable precision and trueness and is determined using the total analytical error (TAE) and an approach based upon the difference between two measurements. The TAE for HIV-1 VL XC was calculated using estimates determined through analysis of data from the LoD study (WHO International Standard) and data from testing performed on three HIV-1 subtype B clinical specimens in K2 EDTA plasma (value assigned with a CE-marked HIV-1 Viral Load test) at a concentration of 40 HIV-1 RNA copies/mL using two kit lots with 16 replicates per kit lot.

TAE was estimated with the Westgard model according to CLSI guideline with the criterion, [(Absolute Bias) + 2 SDs) ≤ 1 $\log_{10}$ copies/mL].[9] The difference between two measurements approach was evaluated with the criterion, [(2 x SQRT(2) x SD) ≤ 1 $\log_{10}$ copies/mL].

The LLoQ analyses for each specimen are presented in Table 4. The result demonstrates that the HIV-1 VL XC test can determine 40 copies/mL HIV-1 RNA with an acceptable trueness and precision.

Table 4. Determination of the LLoQ for the HIV-1 VL XC Test

HIV-1 Subtype B Sample	Kit Lot	N	Nominal HIV-1 Conc. ($\log_{10}$ copies/mL)	Observed HIV-1 Conc. ($\log_{10}$ copies/mL)	Bias	Total SD	Total Analytical Error[a]	Two Measurement Approach[b]
WHO	1	24	1.60	1.51	-0.09	0.14	0.37	0.39
	2	24	1.60	1.48	-0.12	0.17	0.47	0.49
	3	24	1.60	1.56	-0.04	0.31	0.65	0.87

HIV-1 Subtype B Sample	Kit Lot	N	Nominal HIV-1 Conc. (log_{10} copies/mL)	Observed HIV-1 Conc. (log_{10} copies/mL)	Bias	Total SD	Total Analytical Error[a]	Two Measurement Approach[b]
Clinical Specimen 1	1	16	1.60	1.65	0.05	0.10	0.25	0.29
	2	16	1.60	1.63	0.03	0.11	0.25	0.32
Clinical Specimen 2	1	16	1.60	1.80	0.20	0.12	0.44	0.35
	2	16	1.60	1.73	0.13	0.12	0.37	0.34
Clinical Specimen 3	1	16	1.60	1.45	-0.15	0.29	0.72	0.81
	2	16	1.60	1.62	0.02	0.16	0.33	0.45

[a] TAE calculated according to the Westgard model where [TAE = $|\text{Bias}| + (2\times SD) \le 1$ log_{10} copies/mL] ensuring there is a 95% probability that the measurement will be less than 1 log_{10} copies/mL from the true value.
[b] Two measurements approach [$2 \times (SQRT(2) \times SD) \le 1$ log_{10} copies/mL] indicates that a difference of less than 1 log_{10} copies/mL can be explained by a random measurement error.

18.3 Precision/Reproducibility

The precision and reproducibility of the HIV-1 VL XC test was established in a three-site, blinded study using a seven-member panel of HIV-1 reference material spiked into HIV-1 negative EDTA plasma with RNA concentrations that span the HIV-1 VL XC test quantitation range. Two operators at each of the three study sites tested one panel of seven samples twice per day over six testing days. Two sites used GeneXpert Dx instruments and one site used an Infinity-80 instrument. Three kit lots of the HIV-1 VL XC test were used in the study. The precision/reproducibility study was evaluated in accordance with CLSI guideline.[10]

The reproducibility of the HIV-1 VL XC test was evaluated by using nested ANOVA with terms for Site/Instrument, Lot, Operator, Day, Run, and Within-Run. The standard deviation and the percentage of variability due to each component of the log_{10} HIV-1 transformed concentrations were calculated (see Table 5).

Table 5. HIV-1 VL XC Test Contribution to Total Variance and Total Precision

Expected HIV-1 RNA Concentration (copies/mL)	N	Mean[a]	Variance Source													
			Site		Lot		Operator		Day		Run		Within-Run		Total	
			SD[b]	(%)	SD	(%)	SD	(%)	SD	(%)	SD	(%)	SD	(%)	SD	CV (%)[c]
40 cp/mL	143[d]	1.59	0.01	0.55	0.03	2.15	0.04	5.97	0.05	7.80	0.00	0.00	0.16	83.53	0.17	10.69
200 cp/mL	144	2.28	0.02	5.52	0.03	9.27	0.01	2.08	0.00	0.00	0.00	0.00	0.09	83.14	0.10	4.39
$1x10^3$ cp/mL	144	2.99	0.00	0.00	0.02	9.75	0.00	0.00	0.02	13.86	0.00	0.00	0.06	76.38	0.06	2.01
$1x10^4$ cp/mL	144	3.98	0.01	4.72	0.02	15.66	0.00	0.00	0.00	1.00	0.01	6.19	0.04	72.43	0.05	1.26
$1x10^6$ cp/mL	143[e]	6.01	0.01	3.40	0.03	15.35	0.00	0.00	0.00	0.00	0.00	0.00	0.06	81.25	0.07	1.16
$1x10^7$ cp/mL	144	6.96	0.00	0.00	0.04	17.70	0.00	0.00	0.03	10.97	0.00	0.00	0.09	71.32	0.10	1.44

[a] Mean HIV-1 RNA cp/mL log_{10}
[b] SD in log_{10}
[c] CV = (total SD/mean)*100
[d] 1 sample with "HIV-1 Not Detected" result was excluded
[e] 1 sample with "Error" result was excluded

18.4 Linear Range

The linear range of the HIV-1 VL XC test was determined by analysis of a nine-member panel ranging from 15 copies/mL to 1.2 x 10^7 copies/mL prepared by parallel dilutions of HIV-1 reference material (HIV-1 subtype B) in HIV-1 negative K2 EDTA plasma. The reference material used was calibrated to the WHO 4th International standard for HIV-1 (NIBSC code: 16/194). The panel was tested using two kit lots of the HIV-1 VL XC test, resulting in total 24 or 48 replicates per panel member.

The linearity analysis was performed according to CLSI guideline.[11] The results are presented in Figure 9. The HIV-1 VL XC test is linear from 20 copies/mL to 1x10^7 copies/mL with an R^2>99.

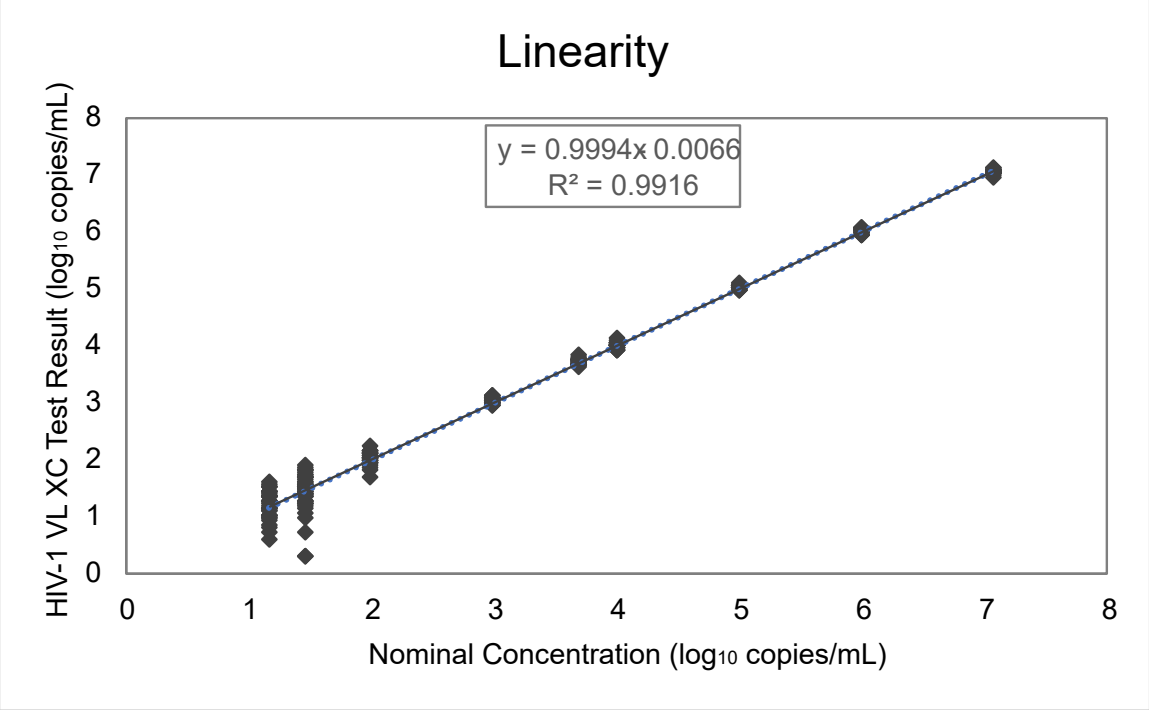


Figure 9. Linearity for the HIV-1 VL XC Test

18.5 Analytical Reactivity (Inclusivity)

The analytical reactivity (inclusivity) for the HIV-1 VL XC test was demonstrated by testing HIV-1 Group M, subtypes A, B, C, D, F, G, H, J, K, CRF-A/B, CRF-A/E, CRF-A/G, CRF-B/C, CRF-06, group N, group O and group P at multiple concentration levels spanning the test's quantitative range of 40-1x10^7 copies/mL depending on subtype/group. Each concentration level was tested in replicates of minimum eight using two kit lots of the HIV-1 VL XC test. The mean $\log_{10}$ concentration obtained for each subtype/group and concentration level was quantified within ± 0.5 $\log_{10}$ of the assigned input concentration and each linear regression had an R2 >0.98 (see Table 6, Table 7, and Table 8).

Table 6. Analytical Reactivity (Inclusivity) for the HIV-1 VL XC Test, HIV-1 Group M subtypes

HIV-1 Group M subtype	Nominal Concentration ($\log_{10}$ copies/mL)	HIV-1 VL XC Result ($\log_{10}$ copies/mL)	Delta ($\log_{10}$ copies/mL)	R^2
A	6.0	5.91	0.09	0.996
	4.0	3.99	0.01	
	2.0	2.02	-0.02	
	1.3	1.37	-0.07	
B	7.0	7.02	-0.02	0.998
	5.0	5.12	-0.12	

HIV-1 Group M subtype	Nominal Concentration (log_{10} copies/mL)	HIV-1 VL XC Result (log_{10} copies/mL)	Delta (log_{10} copies/mL)	R^2
	3.0	3.14	-0.14	
	1.3	1.34	-0.04	
C	6.0	5.89	0.11	0.994
	4.0	3.99	0.01	
	2.0	2.03	-0.03	
	1.3	1.33	-0.03	
D	6.0	5.83	0.17	0.995
	4.0	3.93	0.07	
	2.0	2.00	0.00	
	1.3	1.39	-0.09	
F	6.0	5.74	0.26	0.988
	4.0	3.83	0.17	
	2.0	1.79	0.21	
	1.3	1.12	0.18	
G	6.0	5.89	0.11	0.994
	4.0	3.92	0.08	
	2.0	1.95	0.05	
	1.3	1.16	0.14	
H	5.0	4.92	0.08	0.988
	4.0	3.94	0.06	
	2.0	1.99	0.01	
	1.3	1.52	0.08	
J	2.3	2.36	-0.05	NA[a]
	2.0	2.05	-0.05	
	1.3	1.42	-0.12	
K	4.0	3.86	0.14	0.980
	3.0	2.84	0.16	
	2.0	1.90	0.10	
	1.3	1.11	0.19	

[a] Linear regression analysis was not performed for HIV-1 Group M subtype J and CRF-A/B due to unavailability of specimens spanning a large concentration range.

Table 7. Analytical Reactivity (Inclusivity) for the HIV-1 VL XC Test, HIV-1 CRF's

HIV-1 CRF	Nominal Concentration (log_{10} copies/mL)	HIV-1 VL XC Result (log_{10} copies/mL)	Delta (log_{10} copies/mL)	R^2
CRF-A/B	2.3	2.39	-0.09	NA[a]
	2.0	1.97	0.03	
	1.3	1.32	-0.02	
CRF-A/E	6.0	5.95	0.05	0.992
	4.0	3.97	0.03	
	2.0	1.96	0.04	
	1.3	1.11	0.19	
CRF-A/G	6.0	5.87	0.13	0.991
	4.0	3.90	0.10	
	2.0	1.86	0.14	
	1.3	1.13	0.17	
CRF-B/C	6.0	5.70	0.30	0.995
	4.0	3.74	0.26	
	2.0	1.81	0.19	
	1.3	1.11	0.19	
CRF-06	7.0	6.94	0.06	0.997
	5.0	5.04	-0.04	
	3.0	3.05	-0.05	
	1.3	1.24	0.06	

[a] Linear regression analysis was not performed for HIV-1 Group M subtype J and CRF-A/B due to unavailability of specimens spanning a large concentration range.

Table 8. Analytical Reactivity (Inclusivity) for the HIV-1 VL XC Test, HIV-1 Group N, Group O and Group P

HIV-1 Group	Nominal Concentration (log_{10} copies/mL)	HIV-1 VL XC Result (log_{10} copies/mL)	Delta (log_{10} copies/mL)	R^2
N	7.0	6.78	0.22	0.994
	5.0	4.84	0.16	
	3.0	2.88	0.12	
	1.3	1.26	0.04	
O	6.0	5.96	0.04	0.995
	4.0	4.07	-0.07	
	2.0	2.12	-0.12	
	1.3	1.54	-0.24	
P	5.0	5.17	-0.17	0.996

HIV-1 Group	Nominal Concentration (log_{10} copies/mL)	HIV-1 VL XC Result (log_{10} copies/mL)	Delta (log_{10} copies/mL)	R^2
	4.0	4.21	-0.21	
	2.0	2.21	-0.21	
	1.3	1.51	-0.21	

In addition, analytical reactivity (inclusivity) for the HIV-1 VL XC test was demonstrated by testing HIV-1 specimens as shown in Table 9, representing HIV-1 Group M, subtypes A, B, C, D, F, G, H, J, K, CRF-A/E, CRF-A/G, CRF-B/C, group N and Group O. Each specimen was diluted to 3xLLoQ in K2 EDTA plasma and tested with one kit lot of the HIV-1 VL XC test. All samples tested at 3xLLoQ were reported as HIV-1 detected (Table 9).

Table 9. HIV-1 Specimens Tested at 3xLLoQ

HIV-1 Group	Subtype/CRF	Number of Samples Tested	Number of Samples Reported as HIV-1 Detected
M	A	10	10
	B	10	10
	C	10	10
	D	10	10
	F	10	10
	G	10	10
	H	10	10
	J	4	4
	K	8	8
	CRF-A/E	10	10
	CRF-A/G	11	11
	CRF-B/C	5	5
N	NA	1	1
O	NA	10	10

18.6 Analytical Specificity (Exclusivity)

The analytical specificity of the HIV-1 VL XC test was evaluated by adding potentially cross-reactive or interfering organisms at a concentration of 1 x 10^6 CFU/mL for microorganisms, or 1 x 10^5 copies/mL or $TCID_{50}$ for viruses into HIV-1 negative K2 EDTA plasma and K2 EDTA plasma containing HIV-1 reference material at a concentration of approximately 3xLLoQ. The HIV-1 reference material used was calibrated to the WHO 4th International standard for HIV-1 (NIBSC code: 16/194). Tested organisms are shown in Table 10. None of the tested organisms showed cross-reactivity or interfered with the quantification of the HIV-1 VL XC test.

Table 10. Analytical Specificity Organisms

Virus	Bacteria	Fungi/Yeast	Parasites
Chikungunya virus	*Mycobacterium tuberculosis*	*Candida Albicans*	Leishmania Major
Cytomegalovirus	*Propionibacterium acnes*	*Candida Glabrata*	Plasmodium Falciparum
Epstein-Barr virus	*Staphylococcus aureus*	*Candida Tropicalis*	Trypanosoma brucei
Hepatitis A virus	*Staphylococcus epidermidis*	Pneumocystis *jirovecii*	Trypanosoma cruzi
Hepatitis B virus	*Staphylococcus haemolyticus*		
Hepatitis C virus			
Herpes simplex virus 1			
Herpes simplex virus 2			
Human Herpesvirus 6			
Human Immunodeficiency virus 2			
Human T-cell lymphotropic virus type 1			
Human T-cell lymphotropic virus type 2			
Influenza virus A			

18.7 Potentially Interfering Substances

The susceptibility of the HIV-1 VL XC test to interference by elevated levels of endogenous substances, by drugs prescribed to HIV-1 infected patients or for those who may have co-infections or other co-morbidity, and autoimmune disease markers was evaluated. The inhibitory effects were evaluated in presence and absence of HIV-1 reference material at a concentration of approximately 3xLLoQ. The HIV-1 reference material used was calibrated to the WHO 4th International standard for HIV-1 (NIBSC code: 16/194).

Elevated levels of the endogenous substances shown in Table 11 were shown to not interfere with the quantification of the HIV-1 VL XC test or impact the specificity of the test when tested in presence and absence of HIV-1 RNA. All specimens tested in presence of HIV-1 RNA and the endogenous substance was quantified within ± 0.5 $\log_{10}$ copies/mL of the HIV-1 positive reference specimen. All specimens tested in absence of HIV-1 RNA were reported as HIV-1 Not Detected demonstrating that there was no impact on the specificity of the HIV-1 VL XC test.

Table 11. Endogenous Substances and Concentration Tested

Substance	Tested Concentration
Albumin	9 g/dL
Bilirubin	40 mg/dL
Hemoglobin	1000 mg/dL
Human DNA	0.4 mg/dL
Triglycerides	3000 mg/dL

The drug components as shown in Table 12 were shown to not interfere with the quantification or impact the specificity of the HIV-1 VL XC test when tested at three times peak level concentration (C_{max}) in the presence and absence of HIV-1 RNA.

Table 12. Drug Pools Tested

Pool	Drugs
1	Zidovudine, Clarithromycin, Interferon alfa-2b, Maraviroc, Rilpivirine, Ganciclovir
2	Abacavir sulfate, Peginterferon 2a, Ribavirin, Emtricitabine, Adefovir dipivoxil, Entecavir, Valganciclovir HCl
3	Tenofovir disoproxil fumarate, Lamivudine, 3TC, Raltegravir, Etravirine
4	Stavudine, d4T, Efavirenz, Lopinavir, Ciprofloxacin, Indinavir sulfate, Acyclovir
5	Nevirapine, Azithromycin, Telbivudine, Foscarnet[a], Cidofovir
6	Fosamprenavir calcium, Elvitegravir, Darunavir, Cobicistat, Atazanavir
7	Paritaprevir, Simeprevir
8	Daclatasvir, Elbasvir, Ledipasvir, Ombitasvir, Glecaprevir, Velpatasvir, Dasabuvir
9	Dolutegravir, Bictegravir, Doravirine, Maraviroc
10	Acetaminophen, Acetylsalicylic acid, Atorvastatin, Loratadine
11	Nadolol, Ascorbic acid, Phenylephrine, Ibuprofen
12	Artemether, Desethylamodiaquine, Mefloquine, Quinine
13	Primaquine, Chloroquine, Doxycycline
14	Rifampin, INH, Ethambutol, Pyrazinamide
15	Moxifloxacin, Levofloxacin, Amikacin, Bedaquiline[a]
16	Trimethoprim/Sulfamethoxazole, Gentamicin, Metronidazole, Ceftriaxone

[a] Tested individually instead of in combination with other drug components

Testing of K2 EDTA plasma specimens from five individuals positive for each of the autoimmune disease markers; systemic lupus erythematosus (SLE), anti-nuclear antibodies (ANA) or rheumatoid factor (RF) were shown to not interfere with the quantification of the HIV-1 VL XC test or impact the specificity of the test when tested in presence and absence of HIV-1 RNA.

18.8 Matrix Equivalency (K2 EDTA and PPT-EDTA)

Matrix equivalency for the HIV-1 VL XC test was conducted with matched clinical specimens from 50 HIV-1 positive individuals and 25 HIV-1 negative blood donors collected in K2 EDTA and PPT-EDTA collection tubes. The HIV-1 titers of the matched specimens (K2 EDTA and PPT-EDTA) from HIV-1 positive individuals covered the quantitative range of the test, 40-1x10^7 copies/mL.

Matrix equivalency for the HIV-1 VL XC test was demonstrated as shown in Figure 10. All HIV-1 positive specimens collected in PPT-EDTA media produced concentrations of HIV-1 RNA within ± 0.5 $\log_{10}$ copies/mL of the HIV-1 positive specimen collected in K2 EDTA media when tested with the HIV-1 VL XC test. All 25 matched HIV-1 negative specimens were reported as HIV-1 Not Detected.

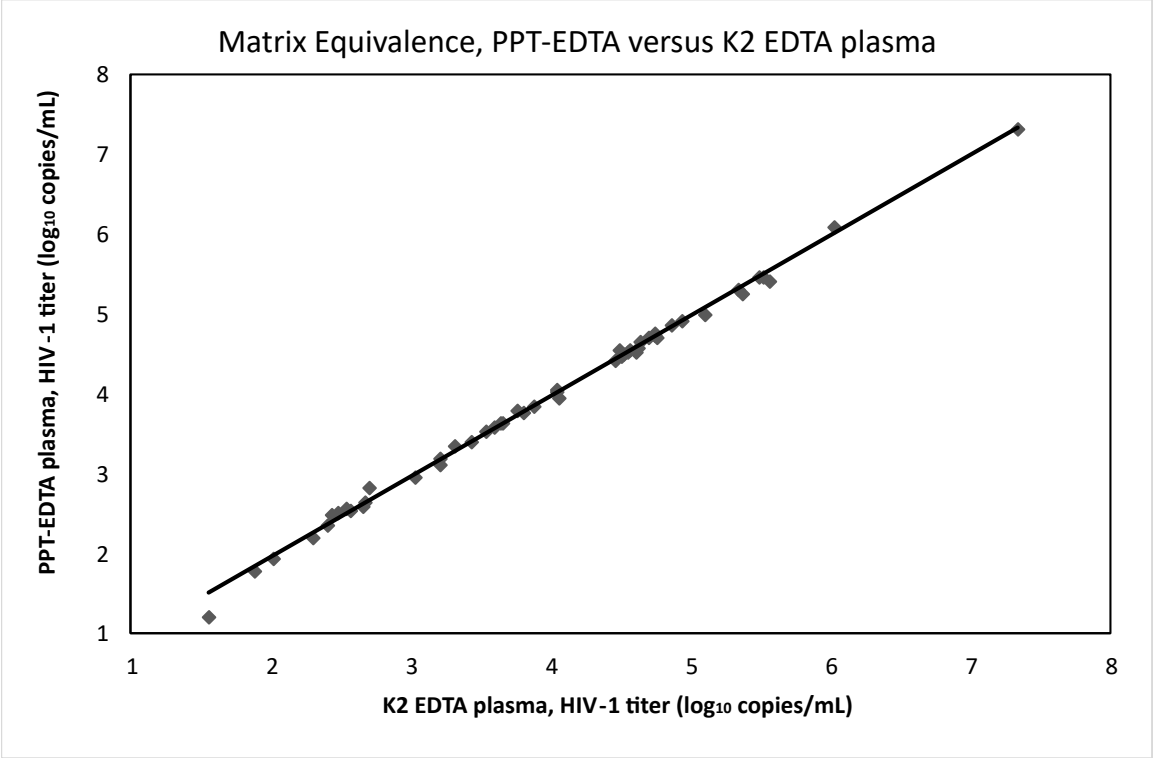


Figure 10. Linear Regression of HIV-1 titer (log_{10} copies/mL), PPT-EDTA plasma versus K2 EDTA plasma

18.9 Whole System Failure Rate

The whole system failure rate for the HIV-1 VL XC test was determined by testing 100 replicates of K2 EDTA plasma spiked with a HIV-1 subtype B specimen calibrated to the WHO 4th International Standard for HIV-1 (NIBSC code 16/194). The K2 EDTA plasma was spiked to a target concentration of 60 copies/mL and tested with one kit lot of the HIV-1 VL XC test.

The results of this study showed that all 100 replicates were valid and reported HIV-1 positive, resulting in a whole system failure rate of 0%.

18.10 Carry Over Contamination

A high titer HIV-1 positive specimen (>1 x 10^7 copies/mL) was tested, immediately followed by testing a HIV-1 negative specimen in the same GeneXpert instrument module. The procedure was repeated twenty (20) times in two different modules. The carryover rate for the HIV-1 VL XC test was 0%.

19 Performance Characteristics – Clinical Performance

19.1 Specificity

The specificity of the HIV-1 VL XC test was evaluated using 500 EDTA plasma specimens from HIV-1 negative blood donors. None of the 500 specimens tested were detected by the HIV-1 VL XC test equating to 100% specificity (95% CI = 99.2-100.0).

19.2 Method Correlation

A multi-site study was conducted to evaluate the performance of the HIV-1 VL XC test relative to a nucleic acid amplification test (NAAT) comparator method using fresh and frozen human plasma specimens collected from known HIV-1 infected individuals. Of the 362 specimens, each from unique individuals, 206 (56.9%) were collected from male subjects. Most individuals (94.5%; 342/362) were in the age range of 22 to 59 years. Classification of specimens by HIV-1 Group M subtypes in this study population were shown to be 25.1% subtype B, 16.1% non-B subtype and 58.8% subtype unknown.

There were 21 indeterminate results of which 14 were resolved after retesting. The final indeterminate rate was 1.93% (7/362).

Of the 362 specimens, 328 were within the quantitation range of Xpert HIV-1 VL XC and the comparator test. The Deming regression shows high correlation between the Xpert HIV-1 VL XC test and the comparator method with a slope of 0.9625 and intercept of 0.0198. The R2 was 0.9561.

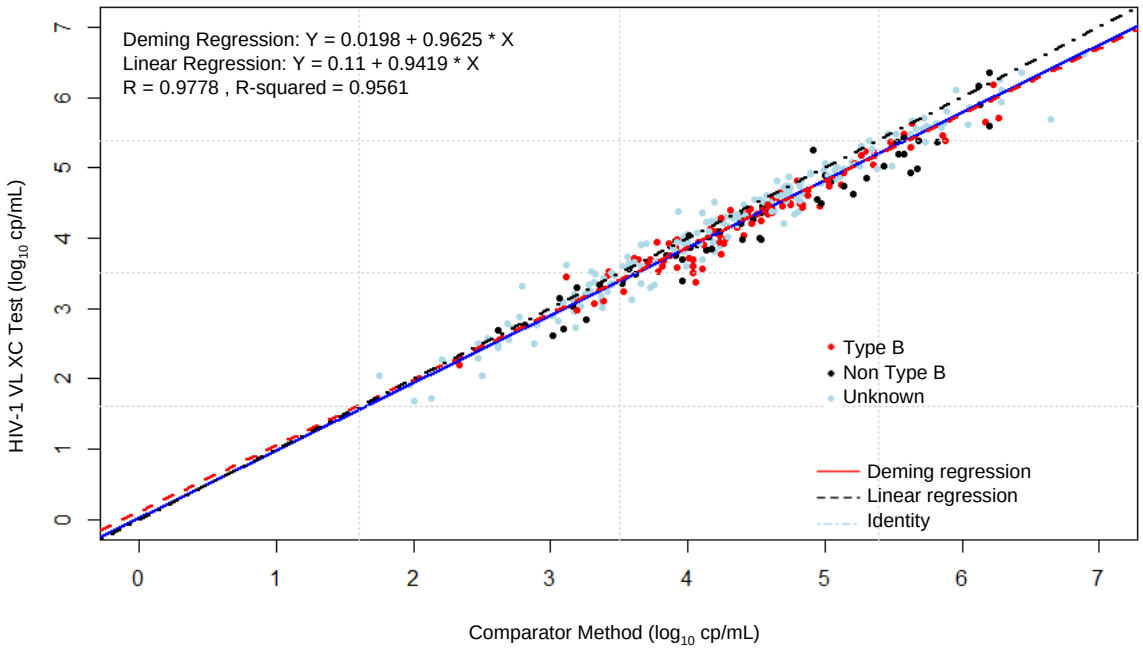


Figure 11. Correlation between the HIV-1 VL XC Test Relative to a Comparator Method

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22 Technical Assistance

Before Contacting Us

Collect the following information before contacting Cepheid Technical Support:

- Product name
- Lot number
- Serial number of the instrument
- Error messages (if any)
- Software version and, if applicable, Computer Service Tag Number

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Contact information for all Cepheid Technical Support offices is available on our website:www.cepheid.com/en/support/contact-us

23 Table of Symbols

Symbol	Meaning
REF	Catalog number
IVD	*In vitro* diagnostic medical device
CE	CE marking – European Conformity
	Do not reuse
LOT	Batch code
	Consult instructions for use
	Manufacturer
	Country of manufacture
Σ	Contains sufficient for *n* tests
CONTROL	Control
	Expiration date
°C	Temperature limitation
	Biological risks
	Caution
	Warning

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