

## WHO Prequalification of In Vitro Diagnostics PUBLIC REPORT

**Product: Xpert HIV-1 Qual Assay**  
**WHO reference number: PQDx 0259-070-00**

**Xpert HIV-1 Qual Assay** with **GeneXpert Dx**, **GeneXpert Infinity-48s**, and **GeneXpert Infinity-80**, product code **GXHIV-QA-CE-10**, manufactured by **Cepheid AB**, **CE marked regulatory version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 13 June 2016.

### Summary of WHO prequalification assessment for Xpert HIV-1 Qual Assay

	Date	Outcome
<b>PQ listing</b>	13 June 2016	listed
<b>Dossier review</b>	N/A	N/A
<b>Site inspection(s) of the quality management system</b>	23-25 June 2015	MR
<b>Product performance evaluation</b>	9 May 2016	MR

MR: Meets requirements

N/A: Not applicable

### Report amendments and product changes

This public report has since been amended. Amendments may have arisen because of changes to the prequalified product for which the WHO has been notified and has undertaken a review. Amendments to the report are summarized in the following table, and details of each amendment are provided below.

Version	Summary of amendment	Date of report amendment
2.0	Changes were made to improve product stability, robustness and quantification of HIV-1 rare polymorphisms in group M.	29 June 2017
3.0	Addition of a defined intended end user and consequently updated instructions for use.	19 April 2018

4.0	Addition of a new IVD system, the GeneXpert Edge System, for use with Cepheid Xpert assays. The change includes new instructions for the use of the GeneXpert Edge System with the new operating software, Edge Software Version 1.0. Cepheid's notified body changed from LRQA (UK) to BSI (Netherlands). Labels and IFUs were updated accordingly.	6 June 2019
5.0	Addition of a new GeneXpert DX instrument product codes for use with all prequalified assays. New GeneXpert DX instrument models use GeneXpert modules, which have 10-channel optical system modules, compared to the 6-channel optical system that pre-existed.	3 December 2020
6.0	Extension of shelf-life of kit to 24 months; nonreportable changes to the IFU (P/N: 301-3048 include revision of technical support contact information and revision level changes for the IFU due to the introduction of new language translations. Addition of the statement in the commitments section of the public report that the WHO did not evaluate commitments 2 to 4 as the information had not been provided.	15 May 2023

**Intended use:**

According to the claim of Cepheid AB, *"the HIV-1 Qual assay, performed on the GeneXpert Instrument Systems, is a qualitative in vitro diagnostic test designed to detect Human Immunodeficiency Virus Type 1 (HIV-1) total nucleic acids on the automated GeneXpert Systems using human whole blood (WB) and dried blood spot (DBS) specimens from individuals suspected of HIV-1 infection and is validated for specimens across Group M (subtypes A, B, C, D, F, G, H, J, K, CRF01\_AE, CRF02\_AG, and CRF03\_AB), Group N, and Group O. The HIV-1 Qual assay is intended to aid in the diagnosis of HIV-1 infection in conjunction with clinical presentation and other laboratory markers. The assay is intended to be used by laboratory professionals or specifically-trained healthcare workers. The assay is not intended to be used as a blood donor screening test for HIV-1"*.

**Assay description:**

According to the claim of Cepheid AB, *"The GeneXpert Instrument Systems automate and integrate specimen preparation, nucleic acid extraction and amplification, and detection of the target sequence in simple or complex specimens using real time reverse transcription PCR (RT-PCR). The systems consist of an instrument, personal computer, and preloaded*

software for performing tests and viewing the results. The systems require the use of single-use disposable GeneXpert cartridges that hold the RT-PCR reagents and host the RT-PCR processes. Because the cartridges are self-contained, cross-contamination between specimens is minimized.

For a full description of the system, see the GeneXpert Dx System Operator Manual or the GeneXpert Infinity System Operator Manual.

Xpert HIV-1 Qual assay includes reagents for the detection of HIV-1 total nucleic acids in specimens as well as an internal control to ensure adequate processing of the target and to monitor the presence of inhibitor(s) in the RT and PCR reactions. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability".

**Product test kit contents:**

<b>Xpert HIV-1 Qual Assay kit</b>	<b>10 tests (product code GXHIV-QA-CE-10)</b>
HIV-1 Qual Assay Cartridges with Integrated Reaction Tubes	10
HIV-1 Qual Assay Sample Reagent Set (Sample Reagent)	10
Disposable 1 mL Transfer Pipettes	1 bag of 10 per kit
Disposable 100 µL Transfer Micropipettes	1 bag of 10 per kit
CD (includes IFU)	1

**Instrumentation:**

<b>Product name</b>	<b>Product code</b>
<b>Xpert HIV-1 Qual assay</b>	GXHIV-QA-CE-10
<b>Xpert HIV-1 Qual assay with GeneXpert Dx (including barcode scanner and operator manual)</b>	GXI-1-L, GXI-1-D, GXII-1-L, GXII-1-D, GXII-2-L, GXII-2-D, GXIV-1-L, GXIV-1-D, GXIV-2-L, GXIV-2-D, GXIV-3-L, GXIV-3-D, GXIV-4-L, GXIV-4-D, GXXVI-4-L, GXXVI-4-D, GXXVI-8-L, GXXVI-8-D, GXXVI-12-L, GXXVI-12-D, GXXVI-16-L, GXXVI-16-D, GXI-1-D-10C, GXIV-4-D-10C, GXI-1-L-10C, GXIV-4-L-10C, GXII-1-D-

	10C GXXVI-4-D-10C, GXII-1-L-10C GXXVI-4-L-10C, GXII-2-D-10C, GXXVI-8-D-10C, GXII-2-L-10C, GXXVI-8-L-10C, GXIV-1-D-10C GXXVI-12-D-10C, GXIV-1-L-10C, GXXVI-12-L-10C, GXIV-2-D-10C, GXXVI-16-D-10C, GXIV-2-L-10C, GXXVI-16-L-10C, GXIV-3-D-10C, and GXIV-3-L-10C
<b>Xpert HIV-1 Qual assay with GeneXpert Infinity-48s (including barcode scanner and operator manual)</b>	INFINITY48-16, INFINITY48-16-EUROPE, INFINITY48-24, INFINITY48-24-EUROPE, INFINITY48-32, INFINITY48-32-EUROPE, INFINITY48-40, INFINITY48-40-EUROPE, INFINITY48-48, INFINITY48-48-EUROPE
<b>Xpert HIV-1 Qual assay with GeneXpert Infinity-80 (including barcode scanner and operator manual)</b>	INFINITY80-16, INFINITY80-16-230V, INFINITY80-24, INFINITY80-24-230V, INFINITY80-32, INFINITY80-32-230V, INFINITY80-40, INFINITY80-40-230V, INFINITY80-48, INFINITY80-48-230V, INFINITY80-56, INFINITY80-56-230V, INFINITY80-64, INFINITY80-64-230V, INFINITY80-72, INFINITY80-72-230V, INFINITY80-80, INFINITY80-80-230V
<b>Xpert HIV-1 Qual assay with GeneXpert Edge System</b>	GXI-EDGE-L
<b>GeneXpert Dx Software Version 4.6a or higher (GeneXpert Dx systems), Xpertise 4.6 or higher (Infinity-48) or Xpertise 6.2 or higher (Infinity-80/Infinity-48s) GeneXpert Edge System Software version 1.0.</b>	GX4.0SWKIT, XPERTISE-G2-SWKIT

**Items required but not provided for dried blood spot (DBS) collection:**

Item
<b>Consumables:</b> Whatman 903 or Munktell filter paper cards, lancets, desiccants, plastic sealable bags, alcohol swabs, wipes, and bleach
<b>Durables:</b> Sterile scissors, forceps
<b>Equipment:</b> Eppendorf ThermoMixer C (Eppendorf order number 5382 000.015), Eppendorf SmartBlock (Eppendorf order number 5309 000.007)

**Storage:**

The test kit must be stored at 2-28 °C.

**Shelf-life upon manufacture:**

24 months.

**Warnings/limitations:**

1. No HIV-1 reactive clinical specimens were used in studies to determine specimen stability for whole and capillary blood spotted on filter paper. The user should be aware that the stabilities of such specimens have not been proven.
2. In addition, no HIV-1 reactive clinical specimens were used for studies to demonstrate the equivalence of performance using different filter papers. It cannot therefore be assumed that both Whatman 903 and Munktell TFN filter papers perform in the same manner with these specimens.
3. The use of any other filter papers has not been validated.

**Prioritization for prequalification**

Based on the established eligibility criteria, Xpert HIV-1 Qual assay was given priority for WHO prequalification assessment.

**Product dossier assessment**

In accordance with the WHO procedure for abbreviated prequalification assessment, Cepheid AB was not required to submit a product dossier for Xpert HIV-1 Qual assay as per the "Instructions for compilation of a product dossier" (PQDx\_018 v1).

Notwithstanding, certain aspects of the product dossier submitted for stringent regulatory review for the purposes of CE marking were reviewed by a technical expert during the site inspection.

Following this review, several issues of concern for WHO are to be resolved as commitments for prequalification:

1. The manufacturer is required to fully verify the performance of DBS collected on filter paper for use with the assay, as the product design and development verification was found insufficient when using DBS, according to the IFU. This commitment was fulfilled. The issue was closed.
2. Full study data is required on validation of specimen stability when collected as a dried blood spot (DBS), under varying conditions of humidity and temperature. This is required for each claimed filter paper. This study must incorporate, amongst other specimens, clinical specimens that are HIV-1 reactive. The IFU is required to be updated with information reflecting the outcomes of this study.
3. Further specimen stability studies for whole blood and capillary blood spotted on filter paper must be undertaken using HIV-1 reactive clinical specimens.
4. The IFU is required to be updated with the specification (product code) for Whatman 903 and Munktell TFN filter papers.

**NOTE:** WHO did not evaluate the claims covered by commitments 2-4, as the information had not been provided. Procurers should note warnings/limitations stated on page 5 of 42.

## Manufacturing site inspection

A comprehensive desk assessment of Cepheid AB Quality Management System was performed applicable to the site of manufacture (Röntgenvägen 5, SE-171 54 Solna, Sweden (Reagent cartridge manufacture)) of Xpert HIV-1 Qual assay in March 2022 as per the "Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics" (PQDx\_014 v4). The desk assessment found that the manufacturer had an acceptable quality management system and good manufacturing practices in place that ensured the consistent manufacture of a product of good quality.

The manufacturer's responses to the nonconformities found at the time of the inspection were accepted on the 25 of October 2022.

Based on the desk assessment and corrective action plan review, the quality management system for Xpert HIV-1 Qual assay meets WHO prequalification requirements.

*To note:*

Due to the COVID-19 pandemic and the corresponding national and international travel restrictions, some inspection dates may be impacted.

Please see below the link to the official statement of the PQ team regarding the impact of COVID-19 on Prequalification activities:

[https://www.who.int/diagnostics\\_laboratory/eual/impact\\_covid-19\\_PQT/en/](https://www.who.int/diagnostics_laboratory/eual/impact_covid-19_PQT/en/)

## Product performance evaluation

Xpert HIV-1 Qual was evaluated by the NHLS HIV PCR Laboratory, Charlotte Maxeke Johannesburg Academic Hospital, South Africa and the International Laboratory Branch, Division of Global HIV and TB, CDC Atlanta, on behalf of WHO. The evaluation took place from 14 August 2015 to 21 April 2016. From this evaluation, we drew the following conclusions.

Xpert HIV-1 Qual assay is a qualitative nucleic acid amplification assay designed to detect Human Immunodeficiency Virus Type 1 (HIV-1) total nucleic acids on the automated GeneXpert Instrument Systems using human venous or capillary whole blood (WB) and dried blood spot (DBS) specimens from individuals suspected of HIV-1 infection. It is validated for specimens across Group M subtypes A, B, C, D, F, G, H, A/E and A/B, CRF AG/GH, J, K, Group N and Group O. A volume of 100µl of whole blood or a 12mm DBS is needed to perform the assay. This type of assay does not require additional laboratory equipment for whole blood specimens and limited laboratory equipment for DBS specimen processing. It can be performed in laboratories with limited facilities.

### **Analytical specimens:**

The assay detected the following subtypes: A, B, C, D, F, AE, and AG in whole blood and DBS specimens. The total hit rate for 21 replicates in the precision study was 100%.

The limit of detection (LoD) in whole blood specimens was verified. In this evaluation, the LoD was estimated to be 350 copies/mL (95% Fiducial limits: 267 – 610); 602 IU/mL (95% Fiducial limits: 460 – 1050). The limit of detection in dried blood spot specimens was verified. In this evaluation, the LoD was estimated to be 634 copies/mL (95% Fiducial limits: 480 – 1015); 1091 IU/mL (95% Fiducial limits: 826 – 1746).

No carry-over was detected using whole blood or DBS specimens.

**Clinical specimens:**

In this limited performance evaluation, we found, in specimens from infants aged less than 18 months, an initial sensitivity (95% CI) of 98.69% (94.4-99.6) and an initial specificity (95% CI) of 100% (97.55-100.0) compared to the reference results (Roche COBAS AmpliPrep/COBAS TaqMan HIV-1 Qualitative Test, v2.0) for all whole blood specimens tested. For specimens less than 72 hours, the initial results were as follows: sensitivity (95%CI) 98.86% (93.83-99.97) and specificity (95% CI) 100% (97.55-100.0). For DBS specimens, we found an initial sensitivity (95% CI) of 98.69% (94.4-99.6) and an initial specificity (95%CI) of 100% (97.55-100.0) compared to the reference results.

In specimens from individuals older than 15 years of age (whole blood specimens only), we found an initial sensitivity (95% CI) of 96.0% (86.3-99.5) and an initial specificity (95% CI) of 100% (93.3-100.0).

For infant DBS specimens, the initial sensitivity and specificity (95% CI) were 99.34% (96.4-100.0) and 100% (97.6-100.0), respectively.

The final sensitivity and specificity (95% CI) were 98.69% (95.4-99.6) and 100% (97.55-100.0), respectively, for all infant whole blood specimens tested compared to the reference results. The final sensitivity and specificity (95% CI) for whole blood infant specimens less than 72 hours were 98.86% (93.83-99.97) and 100% (97.55-100.0), respectively.

For infant DBS specimens, the final sensitivity and specificity (95% CI) were 99.34% (96.4-100.0) and 100% (97.6-100.0), respectively.

In specimens from individuals older than 15 years of age (whole blood only), we found a final sensitivity (95% CI) of 96.0% (86.3-99.5) and a final specificity (95% CI) of 100% (93.3-100.0). In this study, the invalid rate was 2.2%.

<b>Performance characteristics in comparison with an agreed reference standard</b>		
	<b>Initial (95% CI)</b>	<b>Final (95% CI)</b>
<b>Sensitivity %</b>		
<b>Overall</b> (including specimens older than 72 hours):		
<b>Infant specimens:</b>		
Whole blood	98.69% (94.4-99.6)	98.69% (95.4-99.6)
DBS	99.34% (96.4-100.0)	99.34% (96.4-100.0)



<b>Adult specimens:</b>		
Whole blood	96.0% (86.3-99.5)	96.0% (86.3-99.5)
<b>For specimens less than 72 hours:</b>		
Whole blood	98.86% (93.83-99.97)	98.86% (93.83-99.97)
<b>Specificity %</b>		
<b>Overall including specimens older than 72 hours:</b>		
<b>Infant specimens:</b>		
Whole blood	100% (97.55-100.0)	100% (97.55-100.0)
DBS	100% (97.6-100.0)	100% (97.6-100.0)
<b>Adult specimens:</b>		
Whole blood	100% (93.3-100.0)	100% (93.3-100.0)
<b>For specimens less than 72 hours:</b>		
Whole blood	100% (97.55-100.0)	100% (97.55-100.0)
<b>Invalid rate %</b>	2.2%	

<b>Additional performance characteristics</b>	
<b>Subtype detection</b>	21/21 were correctly classified
<b>Limit of detection using WHO 3<sup>rd</sup> International Reference Standard</b>	<b>Whole blood specimens:</b> 350 copies/ml [95% Fiducial limits: 267 - 610]; 602 IU/ml [95% Fiducial limits: 460 - 1050]. <b>DBS:</b> 634 copies/ml [95% Fiducial limits: 480 - 1015]; 1091 IU/ml [95% Fiducial limits: 826 - 1746].
<b>Carry-over</b>	0%

<b>Key operational characteristics</b>	
Validated specimen types	EDTA venous whole blood, EDTA venous and capillary dried blood specimens
Number of steps	10 for the whole blood test procedure, 11 for the DBS test procedure
Time to result	<b>Whole blood specimens:</b> 1h:35 minutes (preparation and loading: 5 minutes; test: 90 min) <b>DBS specimens:</b> 1h: 55 (preparation and loading: 25 minutes when using non-perforated cards; test: 90 min)
Internal QC	Sample Processing Control (SPC): Armored RNA in the form of a dry bead is included in each cartridge to verify adequate processing of the sample virus.
In-use stability of reagents	Reagents are all contained within the cartridge. Cartridges must be tested a maximum of 30 minutes after the addition of the specimen.

## **Labelling**

- 1. Labels**
- 2. Instructions for use**

### 1. Labels

Kit carton label

010733294000159917YYMMDD101234567890240GXHIV-QA-CE-10



**GeneXpert**



$\Sigma 10$



CE 2797 IVD

## Xpert<sup>®</sup> HIV-1 Qual

**REF** GXHIV-QA-CE-10 

**LOT** 1234567890 

 YYYY MM DD  +28  
+2 °C

 (01)07332940001599  
(17)YYMMDD  
(10)1234567890  
(240)GXHIV-QA-CE-10

 Cepheid AB  
Röntgenvägen 5  
SE-171 54 Solna, Sweden

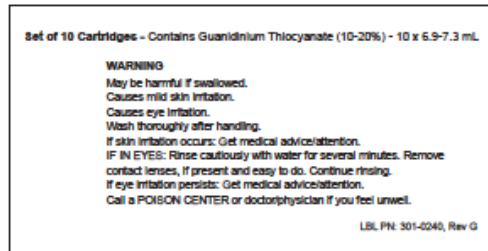
LBL P/N 301-3045, Rev D 

Cartridge label



Figure: cartridge label

**HCV VL, HIV Qual and HIV VL 10-Test Kits**  
**Set of 10 Cartridges - Guanidinium Thiocyanate (10-20%) - 6.9-7.3 mL**  
**Hazard Warning Label**  
Updated 10/11/17



Stock Label p/n 301-0240, Rev G

Material:	Transtherm 1C Paper
Colors:	Black
Adhesive:	AT20
Topcoat:	Full UV Varnish
Label Size:	4.0" x 2.0"
Copy Unwind Position:	#4
General Specifications:	Reference Cepheid Doc D7280 for additional requirements

## **2. Instructions for use<sup>1</sup>**

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<sup>1</sup> English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages.

## **2.1 Getting Started Guide, GeneXpert EdgeSystem**



# Getting Started Guide

GeneXpert® Edge System



## BEFORE YOU BEGIN

Read these instructions completely and carefully.

## INSTALLATION

### GeneXpert Edge System Components



Figure 1. GeneXpert Edge System Components

The GeneXpert Edge System consists of the following:

- 1 GeneXpert Edge Instrument
- 2 AC Power Cord for GeneXpert Edge Instrument
- 3 Ethernet Cable
- 4 Barcode Scanner
- 5 Touch Screen Computer (on the computer stand)
- 6 AC Power Cord/Adapter for Computer
- 7 Small Battery
- 8 AC Power Cord/Adapter for Battery
- 9 Power Strip for Components

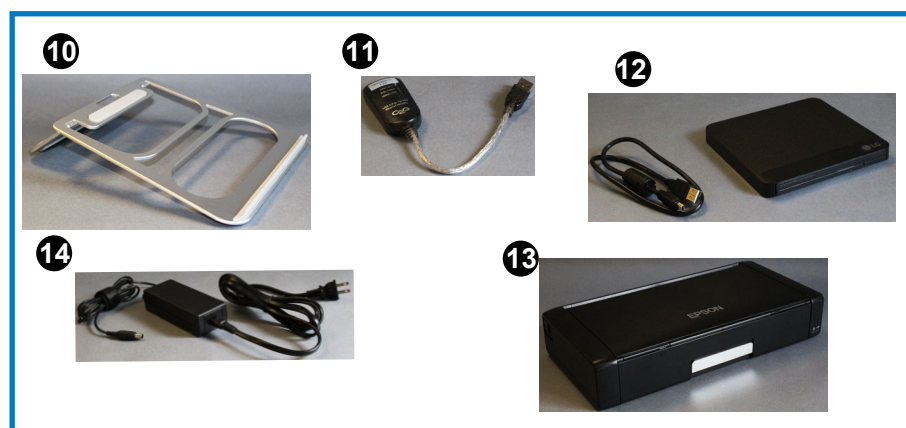


Figure 2. GeneXpert Edge System Accessories

GeneXpert Edge System accessories consist of:

- 10 Computer Stand (Also see Figure 10)
- 11 Ethernet Adapter (For connection to the LIS/Network shipped with the computer)
- 12 External DVD Drive and Cable
- 13 Wireless Printer (Optional)
- 14 Wireless Printer AC Power Cord (Optional)
- 15 Larger Battery (Optional, Not Shown)

### NOTE

Items 10, 11, 12, 13 and 14 may not be required for initial setup. Please store all items not used securely. Refer to the User Guide for accessory component usage.

## UNPACKING THE GeneXpert Edge SYSTEM

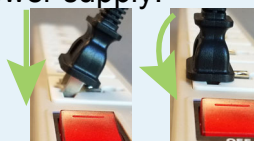
Carefully remove all boxes from the large shipping box. Remove each of the components from their individual packaging.

### NOTE

Be sure to save all packaging material.

## POWER STRIP AND ADAPTER

1. Connect the provided plug adaptor for your location to the Power Strip. Then plug the strip into a local power supply.
2. Insert plugs into the strip at an angle, then rotate the plug so it is square to the strip.



## CHARGING THE BATTERIES

1. Charge the battery fully before use. Do not start a test with 2 bars or less of charge on the small battery 7. Connect the battery cord 8 to the DC In power port on the battery 7. Connect the other end to the power strip 9 and connect to local power to charge. Do not attempt to charge the battery while running a test. Loss of test will occur.

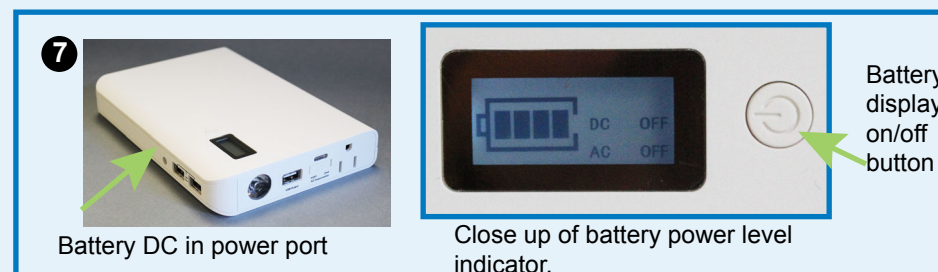


Figure 3. Small Battery Connections

2. Charge the computer battery fully before use. Do not start a test with 50% or less of charge on the computer. Connect the computer AC power cord to the computer port shown in Figure 5. Connect the other end to the power strip 9 and connect to local power.

## CONNECTING THE GeneXpert Edge SYSTEM

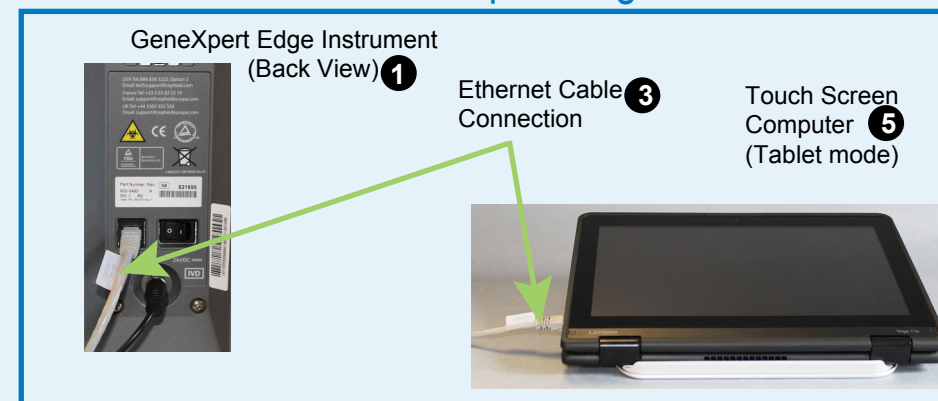


Figure 4. Ethernet Connections

1. Open the computer to tablet mode (see Powering up the GeneXpert Edge System). Connect one end of the supplied Ethernet cable 3 to the Ethernet port on the side of the computer (see Figure 4 and Figure 5). Use the supplied Ethernet cable only.

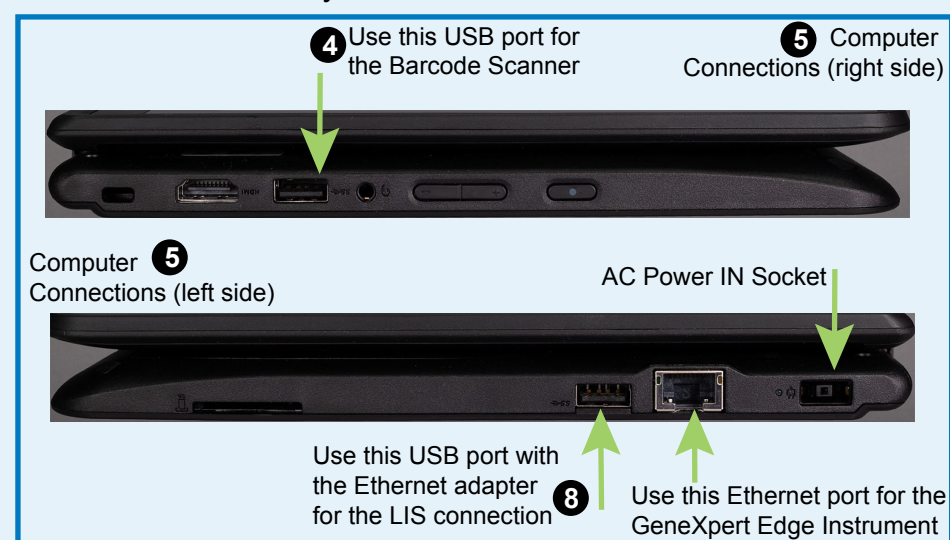


Figure 5. Computer Connections

2. Connect the other end of the Ethernet cable 3 to the Ethernet port on the lower back side of the GeneXpert Edge Instrument 1 as shown in Figure 4 and Figure 6.
3. Connect the barcode scanner 4 USB cable to the USB port on the side of the computer 5 as shown in Figure 5.
4. If an LIS/network connection is required, plug the Ethernet adapter 11 into the USB port shown in Figure 5. Plug the LIS/network cable (not provided) into the Ethernet adapter.

5. Position the GeneXpert Edge 1 so the power switch is accessible (See Figure 6).

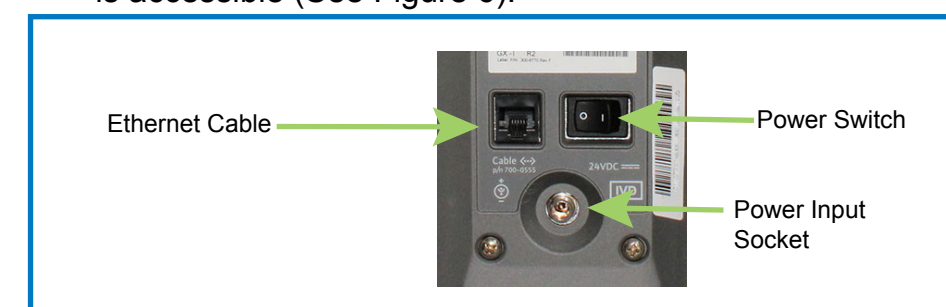


Figure 6. GeneXpert Edge Back Panel

6. Insert the GeneXpert Edge AC power cord 2 into the GeneXpert Edge input socket until it stops. Tighten the knurled nut securely (Figure 6).
7. Connect the other end of the GeneXpert Edge power cord 2 to the battery AC output socket 7 or the power strip. Slide the AC output switch to the ON position.

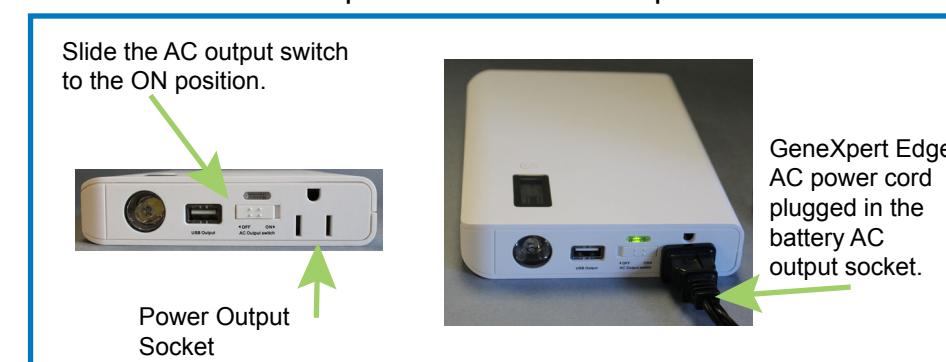


Figure 7. Battery Output Connections

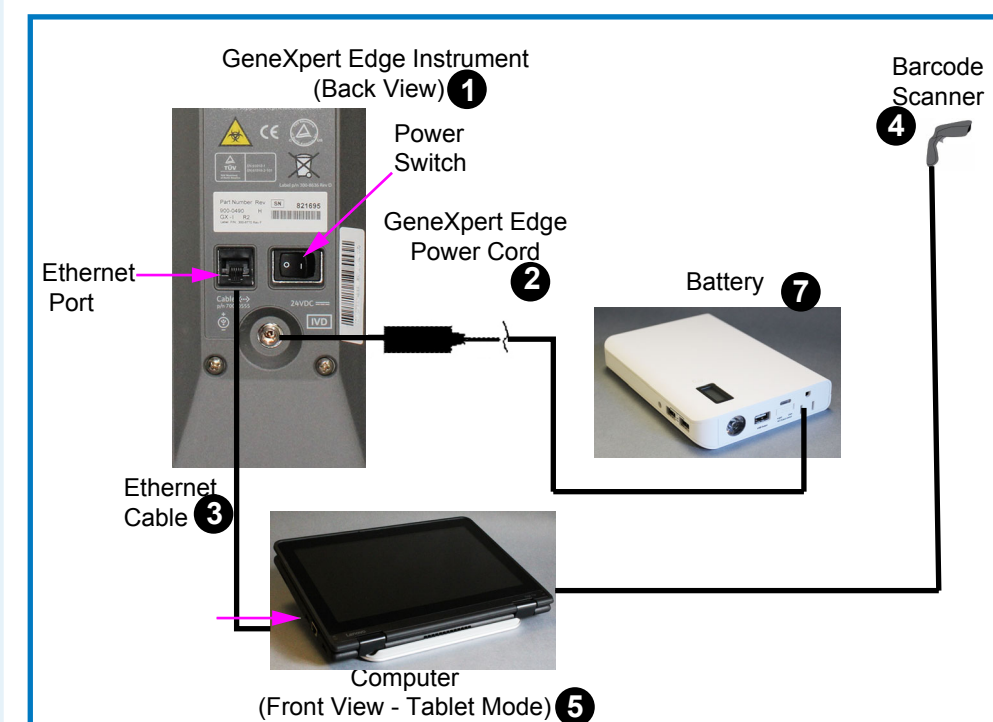


Figure 8. GeneXpert Edge System Connections Overview

### NOTE

Item 11 (Ethernet Adapter for LIS/Network) is not pictured in Figure 8. If used, it can be plugged in where shown by the arrow in the lowest image.



### WARNING

If this system is used in a manner not specified by Cepheid, the safety protection provided by the equipment may be impaired.

### IMPORTANT

Provide at least 5 cm (2 in.) of clearance on each side of the GeneXpert Edge. Do not block the fan exhaust or the air intake on the back side of the instrument. Lack of proper ventilation can cause the GeneXpert Edge to malfunction.





# Getting Started Guide

GeneXpert® Edge System



## POWERING UP THE GeneXpert Edge SYSTEM

1. Reach behind the instrument and press the “|” symbol on the power switch (Figure 6) to turn on the GeneXpert Edge.

The small blue power light on the front of the GeneXpert Edge turns on (Figure 9).

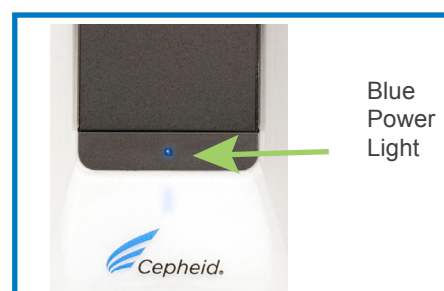


Figure 9. GeneXpert Edge, Blue Power Light

2. Locate the power switch and press to turn on the computer as shown in Figure 10.



Figure 10. Computer Power Switch

### NOTE

The software is configured in Tablet Mode when shipped, however the computer is shipped closed. Gently open the computer display 360 degrees from the closed position, (as shown in Figures 4, 8, and 10).

## STARTING THE SOFTWARE

1. The Windows lock screen will appear after turning on the computer (Figure 11). Touch the screen and swipe upwards.



Figure 11. Windows Lock Screen

2. The Windows Login Screen appears (Figure 12).
3. Touch **Password** field to display the keyboard and then type the password **cphd**, using all lowercase letters.

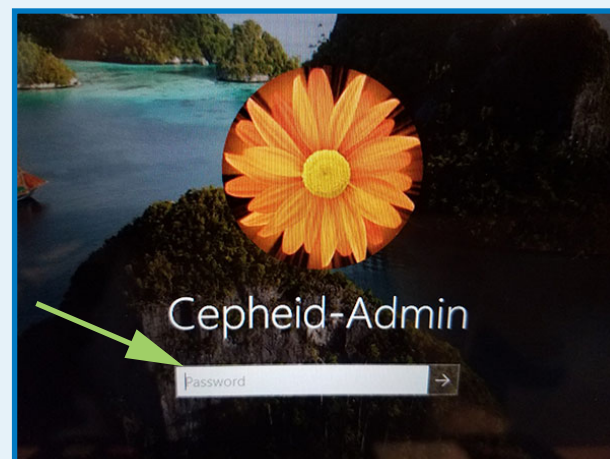


Figure 12. Login Screen

4. Touch the arrow button located at the end of the password entry.
5. The user will be asked to change the Cepheid-Admin password during the first login. Follow the system prompts to change the password.
6. Login to Cepheid-Admin using the new password. Be sure to store the new password in a safe place.
7. The Edge software will open automatically. The Welcome screen appears after the Edge software finishes initializing.
8. Touch the **TOUCH HERE TO BEGIN** button (Figure 13).



Figure 13. Welcome Screen

9. The **RUN NEW TEST** button will appear on the Home screen within 3 minutes (Figure 14). Please be patient as the system initializes.

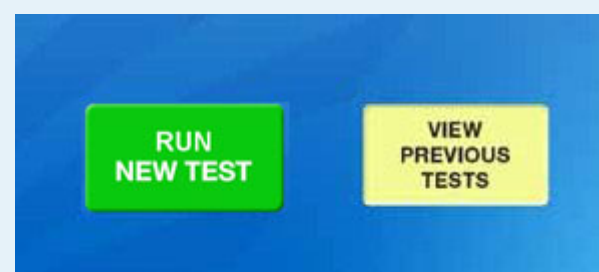


Figure 14. Home Screen with **RUN NEW TEST** Button

10. Verify the battery has charged prior to beginning a test. Do not use the small battery with 2 bars of power or less. Do not use the large optional battery with 50% power or less.
11. Follow instructions for testing samples using the printed Quick Reference Guide included with the Edge system and the Package Insert, included with each assay kit.

### NOTE

Please see the *GeneXpert Edge System User's Guide* for instructions on setting up user logins and passwords.

## CONFIGURING THE ADMINISTRATION FUNCTIONS

See the GeneXpert Edge System User's Guide (P/N 301-9758) for the instructions on the following:

- Creating User Account and Passwords
- Managing Assay Definitions
- Connecting to the Printer (if applicable)

## TROUBLESHOOTING

1. If you do not see the **RUN NEW TEST** button on the Home screen (Figure 14), check that the GeneXpert Edge Instrument front-panel blue light is on (Figure 9) and check that all cables are connected correctly (Figure 8).
2. If you still do not see the **RUN NEW TEST** button on the Home Screen (Figure 14), press the **EXIT** button to return to the Windows Desktop.
3. ① Tap the Application List icon located on the upper left side of the Windows Desktop. ② Then tap the Cepheid folder. ③ Tap the GeneXpert Edge icon.

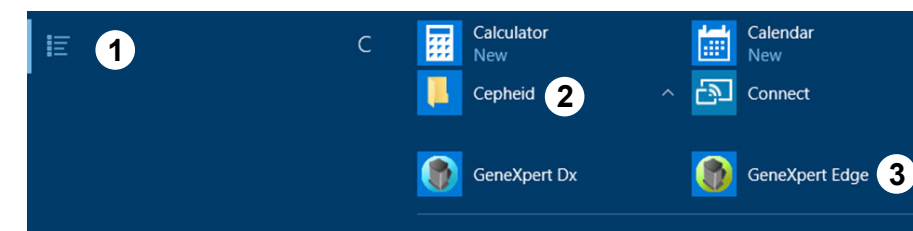


Figure 15. Application List

This will open the Edge software and the Home Screen with the **RUN NEW TEST** button should appear within 3 minutes (Figure 14).

## Cepheid Technical Support

If you need help, please contact Cepheid Technical Support.

Region	Telephone	Email
US	+ 1 888 838 3222	techsupport@cepheid.com
Australia and New Zealand	+ 1800 130 821 + 0800 001 028	techsupportANZ@cepheid.com
Brazil and Latin America	+ 55 11 3524 8373	latamsupport@cepheid.com
China	+ 86 021 5406 5387	techsupportchina@cepheid.com
France	+ 33 563 825 319	support@cepheideurope.com
Germany	+ 49 69 710 480 480	support@cepheideurope.com
India, Bangladesh, Bhutan, Nepal, and Sri Lanka	+ 91 11 48353010	techsupportindia@cepheid.com
Italy	+ 39 800 902 567	support@cepheideurope.com
South Africa	+ 27 861 22 76 35	support@cepheideurope.com
United Kingdom	+ 44 3303 332 533	support@cepheideurope.com
Other European, Middle East, and African countries	+ 33 563 825 319 + 971 4 253 3218	support@cepheideurope.com
Other Countries	+ 1 408 400 8495	techsupport@cepheid.com

## GeneXpert Edge SYSTEM SPECIFICATIONS

### GeneXpert Edge Instrument

- Dimensions: 9.4 cm (3.7 in.) wide, 30.5 cm (12 in.) high, 29.7 cm (11.7 in.) deep.
- Weight: 4 kg (9 lbs).
- Rated AC Voltage Range: 100-240 V ~ 50-60 Hz
- Rated Input Current: 1.5 A @ 100V, 0.7A @ 240V~
- A 100-240 VAC, 50-60 Hz, 10 A, grounded outlet is required.

### Computer

- Dimensions: 300 mm (11.81 in.) wide, 22.90 mm (.9 in.) high, 216 mm (8.5 in.) deep.
- Weight: 1.59 kg (3.5 lbs).
- Rated AC Voltage Range: 100-240 V ~ 50-60 Hz

### Environmental

- Indoor Use Only
- Do not use in direct sunlight
- Operating Temperature: 15-30 °C (59-86 °F)
- Relative Humidity: 10-95% non-condensing



301-3301 Rev. C August 2019

## **2.2 Xpert HIV-1 Qual Instructions for Use**

# Xpert<sup>®</sup> HIV-1 Qual

**REF** GXHIV-QA-CE-10

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Thermomixer<sup>®</sup> is a registered trademark of Eppendorf AG.

SmartBlock<sup>™</sup> is a trademark of Eppendorf AG.

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Cepheid AB  
Röntgenvägen 5  
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Sweden

# Xpert<sup>®</sup> HIV-1 Qual

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For *In Vitro* Diagnostic Use.

## 1 Proprietary Name

Xpert<sup>®</sup> HIV-1 Qual

## 2 Common or Usual Name

HIV-1 Qual

## 3 Intended Use

The HIV-1 Qual assay, performed on the GeneXpert Instrument Systems, is a qualitative *in vitro* diagnostic test designed to detect Human Immunodeficiency Virus Type 1 (HIV-1) total nucleic acids on the automated GeneXpert<sup>®</sup> Systems using human whole blood (WB) and dried blood spot (DBS) specimens from individuals suspected of HIV-1 infection and is validated for specimens across Group M (subtypes A, B, C, D, F, G, H, J, K, CRF01\_AE, CRF02\_AG, and CRF03\_AB), Group N, and Group O.

The HIV-1 Qual assay is intended to aid in the diagnosis of HIV-1 infection in conjunction with clinical presentation and other laboratory markers. The assay is intended to be used by laboratory professionals or specifically-trained healthcare workers.

The assay is not intended to be used as a blood donor screening test for HIV-1.

## 4 Summary and Explanation

Human Immunodeficiency Virus (HIV) is the etiologic agent of Acquired Immunodeficiency Syndrome (AIDS).<sup>1,2,3</sup> It can be transmitted through sexual contact, exposure to infected blood or blood products, prenatal infection of a fetus, or perinatal or postnatal infection of a newborn.<sup>4,5,6</sup> Infected individuals generally develop an acute infection characterized by flu-like symptoms in a period of days to weeks after initial exposure.<sup>7</sup> Acute HIV infections typically last less than 14 days<sup>8</sup> and are associated with high levels of viremia prior to a detectable immune response.<sup>9,10</sup> Therefore, HIV-1 nucleic acid testing can be more sensitive than standard serologic testing in detection of acute infection.<sup>7</sup>

At the end of 2013, there were 35 million (33.2 million–37.2 million) people living with HIV.<sup>11</sup> Of those infected, 2.1 million represent new infections and an estimated 240,000 are children.<sup>11</sup> One-third of all people living with HIV reside in nine countries in southern Africa, which only account for 2% of the global population.<sup>12</sup> Without timely HIV testing and therapy initiation, one-third of HIV-infected infants will die before their first birthday and more than 50% will die before reaching two years old.<sup>11</sup> In contrast, the risk of mortality in children infected with HIV in the U.S. and Europe is only 10–20%.<sup>13</sup> Early diagnosis of HIV infection in infants is a necessity; however, many patients are lost to follow-up while waiting for an early test, usually DNA-PCR, sensitive in the first 18 months of life (which has very limited accessibility) or a rapid test, which is only accurate beginning in the 15 to 18 month age range.<sup>14,15</sup> As a result, HIV-1 nucleic acid testing has been recommended for detecting infection in pediatric patients 18 months of age or younger.<sup>16,17,18,19</sup>

The HIV-1 Qual assay uses reverse transcription polymerase chain reaction (RT-PCR) technology to achieve high sensitivity for the qualitative detection of HIV-1 total nucleic acids in WB or DBS specimen types.

## 5 Principle of the Procedure

The GeneXpert (GX) 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 reverse transcription PCR (RT-PCR). The systems consist of an instrument, personal computer, and preloaded software for performing tests and viewing the results. The systems require the use of single-use disposable GeneXpert cartridges that hold the RT-PCR reagents and host the RT-PCR processes. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the system, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

The HIV-1 Qual assay includes reagents for the detection of HIV-1 total nucleic acids in specimens as well as an internal control to ensure adequate processing of the target and to monitor the presence of inhibitor(s) in the RT and PCR reactions. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.



## 6 Reagents

### 6.1 Materials Provided



The HIV-1 Qual assay kit contains sufficient reagents to process 10 specimens or quality control samples. The kit contains the following:

<b>HIV-1 Qual assay Cartridges with Integrated Reaction Tubes</b>	<b>10</b>
• Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
• Lysis Reagent (Guanidinium Thiocyanate)	1.4 mL per cartridge
• Rinse Reagent	0.5 mL per cartridge
• Elution Reagent	2.5 mL per cartridge
• Binding Reagent	2.4 mL per cartridge
• Proteinase K Reagent	0.48 mL per cartridge
<b>HIV-1 Qual assay Sample Reagent Set (Sample Reagent)</b>	<b>10</b>
• Lysis Reagent (Guanidinium Thiocyanate)	1.0 mL per vial
<b>Disposable 1 mL Transfer Pipettes</b>	<b>1 bag of 10 per kit</b>
<b>Disposable 100 µL Transfer Micropipettes</b>	<b>1 bag of 10 per kit</b>
<b>CD</b>	<b>1 per kit</b>
• Assay Definition Files (ADF)	
• Instructions to import ADF into GeneXpert software	
• Instructions for Use (Package Insert)	

**Note** Safety Data Sheets (SDS) are available at [www.cepheid.com](http://www.cepheid.com) or [www.cepheidinternational.com](http://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 Qual assay cartridges and reagents at 2–28 °C.
- Do not use any reagents that have become cloudy or discolored.
- Do not use a cartridge that has leaked.

## 8 Materials Required but Not Provided

- GeneXpert Dx System or GeneXpert Infinity Systems (catalog number varies by configuration): GeneXpert Instrument, computer with proprietary GeneXpert Dx Software Version 4.7b or higher (GeneXpert Dx systems) or Xpertise 6.4b or higher (Infinity-80/Infinity-48s), barcode scanner, and operator manual.
- Printer: If a printer is needed, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.
- If using DBS:
  - DBS Collection Kit (Filter paper cards, e.g., Whatman 903, Munktell or equivalent, lancets, desiccants, plastic sealable bags, and swabs)
  - Scissors, sterile (recommended for excising DBS from filter paper if not using a perforated DBS card)
  - Forceps
  - Serviette/Wipe
  - Bleach
  - Eppendorf ThermoMixer® C (Eppendorf order number 5382 000.015) (for DBS application only)
  - Eppendorf SmartBlock™ (Eppendorf order number 5309 000.007) (for DBS application only)

## 9 Warnings and Precautions



- Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be treated with standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention<sup>20</sup> and the Clinical and Laboratory Standards Institute.<sup>21</sup>
- Wear protective disposable gloves, laboratory coats, and eye protection when handling specimens and reagents. Wash hands thoroughly after handling specimens and test reagents.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- When processing more than one sample at a time, open only one cartridge; add sample and close the cartridge before processing the next sample. Change gloves between samples.
- Good laboratory practices, including changing gloves between handling patient specimens, are recommended to avoid contamination of specimens or reagents.
- Do not substitute HIV-1 Qual assay reagents with other reagents.
- Do not open the HIV-1 Qual assay cartridge lid except when adding the Sample Reagent and WB or the Sample Reagent-treated DBS sample.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- 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 cartridge lid may yield invalid results.
- Do not use a cartridge that has a damaged reaction tube.



- Each single-use HIV-1 Qual assay cartridge is used to process one specimen. Do not reuse spent cartridges.
- The single-use disposable pipette is used to transfer one specimen. Do not reuse spent disposable pipettes.
- Biological specimens, 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 national or regional disposal procedures. If national or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines.

## 10 Chemical Hazards<sup>23, 24</sup>

- **Signal Word: Warning**
- **UN GHS Hazard Statements:**
  - Harmful if swallowed
  - Causes mild skin irritation
  - Causes eye irritation
- **UN GHS Precautionary Statements:P**
  - Prevention
    - Wash thoroughly after handling.
  - Response
    - 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.
    - Call a POISON CENTER or doctor/physician if you feel unwell.



## 11 Specimen Collection, Transport, and Storage

### 11.1 Whole Blood Collection



Collect WB in sterile tubes using EDTA (lavender top) as the anticoagulant as per the manufacturer's instructions for use. A minimum of 100 µL of WB is required for the HIV-1 Qual assay.

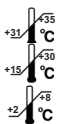


#### Specimen Transport and Storage

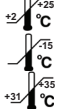
EDTA-anticoagulated WB may be stored at 31–35 °C for up to 8 hours, 15–30 °C for up to 24 hours or at 2–8 °C for up to 72 hours, prior to preparing and testing the specimen.

### 11.2 Dried Blood Spots Collection

Collect DBS specimens using appropriate clinical procedures. DBS should be prepared using Whatman 903 or Munktell filter paper cards or equivalent from blood obtained from a heel-, finger- or toe-stick or collected in an EDTA-tube. DBS are made by spotting blood inside each delineated 12-millimeter circle of the filter paper card. Ensure that the entire circle is covered with blood (approximately 60–70 µL). A minimum of two circles should be made from each specimen to allow for retesting.



If WB was collected in an EDTA-tube, mix the specimen by inverting it 8–10 times before applying it onto the filter. Air-dry the card at room temperature for a minimum of four hours. Package each card in individual resealable bags with a desiccant sachet in each bag. Freshly drawn specimens in EDTA-tubes may be held at 31–35 °C for up to 8 hours, 15–30 °C for up to 24 hours or at 2–8 °C for up to 72 hours, prior to making the DBS.



#### Specimen Transport and Storage

Ship filter paper cards containing DBS to the testing laboratories for further processing in individual resealable bags with a desiccant sachet in each bag. The cards may be stored at 2–25 °C or –15 °C or colder for up to 12 weeks. Cards may also be stored at 31–35 °C for up to 8 weeks.

## 12 Procedure

Before starting, remove the vial containing the Sample Reagent from the kit and, if it was refrigerated, allow to adjust to room temperature. See Figure 1. If the vial has not been stored in an upright position, make sure the buffer is settled in the bottom by giving the vial a firm shake.

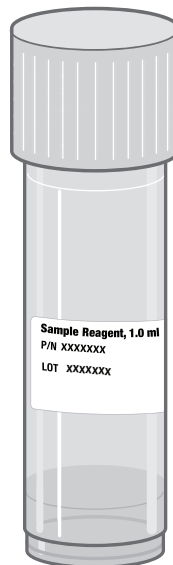


Figure 1. HIV-1 Qual Assay Sample Reagent

## 12.1 Preparing the Cartridge

**Note** There is a thin plastic film that covers the inner ring of 13 ports of the test cartridge. This film should not be removed.

**Important** Start the test within 30 minutes of adding the sample to the cartridge.

### Whole Blood

1. Wear protective disposable gloves.
2. Label the Sample Reagent vial with the specimen identification.
3. Inspect the test cartridge for damage. If damaged, do not use.
4. Open the cartridge lid.
5. Use the 1 mL transfer pipette provided (Figure 2) or an automatic pipette to transfer 750  $\mu$ L of the sample reagent into the sample chamber of the cartridge (Figure 4).

**Note** Allow the Sample Reagent to adjust to room temperature and mix the bottle by inverting before transferring to the cartridge. Transfer exactly 750  $\mu$ L into the sample chamber of the cartridge.

6. Mix the WB sample by inverting the vial (EDTA-microtainer or EDTA (lavender-top) tube) at least seven times. Immediately transfer 100  $\mu$ L using the micropipette provided (see Figure 3) by squeezing the upper bulb and then releasing to aspirate the blood. Squeeze again to dispense the blood into the sample chamber of the cartridge where it will mix with the Sample Reagent already in the sample chamber (Figure 4). Alternatively, use an automatic pipette to dispense the blood into the sample chamber of the cartridge (see Figure 4). Do **NOT** pour the specimen into the chamber!

**Note** Ensure the 100  $\mu$ L of blood is added to Sample Reagent already in the sample chamber.

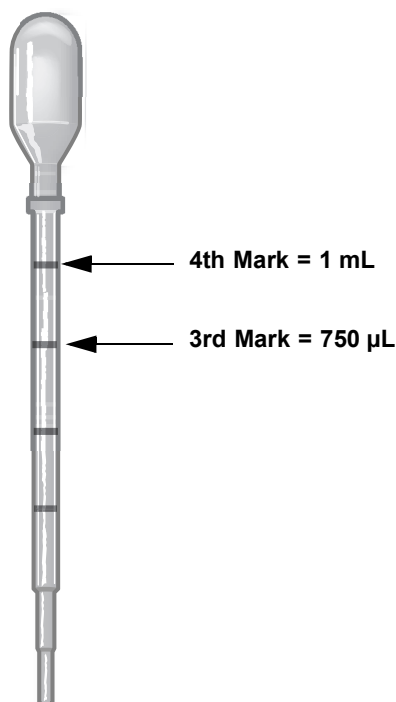


Figure 2. HIV-1 Qual Assay 1 mL Transfer Pipette

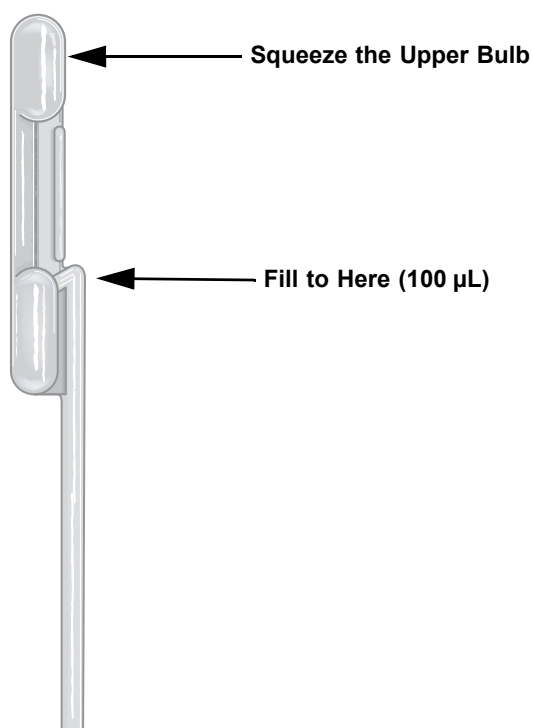


Figure 3. HIV-1 Qual Assay 100 µL Transfer Micropipette

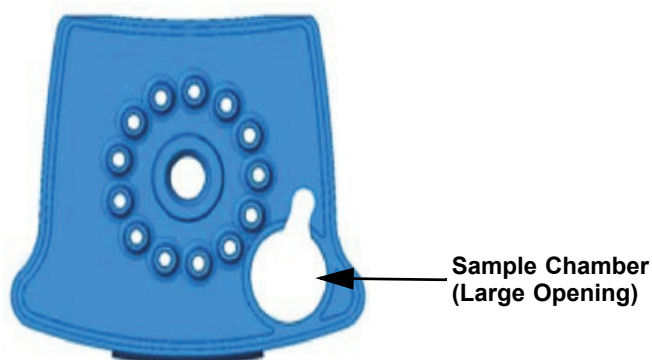


Figure 4. HIV-1 Qual Assay Cartridge (Top View)

#### Dried Blood Spots

**Note**

To prevent cross contamination, clean and wipe off forceps and scissors (if DBS card is not perforated) with a serviette between specimens using 10% bleach in water. Dry the forceps and scissors after each decontamination.

1. Wear protective disposable gloves.
2. Turn on ThermoMixer to heat to 56 °C.
3. Label the Sample Reagent vial with the specimen identification.
4. Using sterilized scissors, excise one entire DBS from the filter paper card for each specimen. Follow the delineated lines when excising the DBS. If perforated circles are used, use forceps to detach the DBS.
5. Unscrew the lid on the vial containing the Sample Reagent and place one DBS in the vial. If DBS does not settle to the bottom, use the backside of the forceps to gently push it down. Ensure that the DBS is fully submerged in the Sample Reagent buffer.
6. Place the vial with the DBS in a ThermoMixer and incubate for 15 minutes at 56 °C while rotating at 500 rpm.

7. Inspect the test cartridge for damage. If damaged, do not use.
8. Open the cartridge lid.
9. Use the 1 mL transfer pipette provided (see Figure 2) or an automatic pipette to transfer all the liquid from the lysed DBS specimen into the sample chamber of the cartridge (see Figure 4). Ensure the pipette is filled above the third mark on the transfer pipette. Avoid suction of the DBS with the pipette. Do **NOT** pour the specimen into the chamber!
10. Close the cartridge lid.

## 12.2 Starting the Test

**Important** Before starting the test, make sure the HIV-1 Qual Assay Definition File (ADF) 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

1. Turn on the GeneXpert instrument system:
  - If using the GeneXpert Dx instrument, first turn on the instrument and then turn on the computer. The GeneXpert software will launch automatically. If it doesn't, 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 doesn't, double click the Xpertise software shortcut icon on the Windows desktop.
2. Log on to the GeneXpert Instrument System software using your user name and password.
3. In the GeneXpert System window, click **Create Test** (GeneXpert Dx) or click **Orders** and **Order Test** (Infinity).
4. Scan in the Patient ID (optional). 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.
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 reports. The Scan Cartridge dialog box appears.
6. Scan the barcode on the HIV-1 Qual assay cartridge. The Create Test window appears. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.
7. Click **Start Test** (GeneXpert Dx) or **Submit** (Infinity). Enter your password, if requested.
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 and removing the cartridge.
- D. The used cartridges should be disposed 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*.

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

**CONTROL** Each test includes a Sample Volume Adequacy (SVA), a Sample Processing Control (SPC) and 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 validated 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 user from resuming the test.
- **Sample Processing Control (SPC):** Ensures that the sample was correctly processed. The SPC is an Armored RNA® in the form of a dry bead that is included in each cartridge to verify adequate processing of the sample virus. The SPC verifies that lysis of HIV-1 has occurred if the organism is present and verifies that the specimen processing is adequate. Additionally this control detects specimen-associated inhibition of the RT-PCR reaction. The SPC should be positive in a negative sample and can be negative or positive in a positive sample. The SPC passes if it meets the validated acceptance criteria.
- **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 it meets the validated acceptance criteria.
- **External Controls:** External controls should be used in accordance with local, state, and federal accrediting organizations' requirements as applicable.

## 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 (see Figure 5 and Figure 6). Possible results are shown in Table 1

**Table 1. HIV-1 Qual assay Results and Interpretation**

Result	Interpretation
<b>HIV-1 DETECTED</b> See Figure 5.	The HIV-1 target nucleic acids are detected. <ul style="list-style-type: none"> <li>• The HIV-1 target nucleic acids have a Ct within the valid range.</li> <li>• SPC: NA (not applicable); SPC is ignored because the HIV-1 target amplification occurred.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>
<b>HIV-1 NOT DETECTED</b> See Figure 6.	The HIV-1 target nucleic acids are not detected. SPC meets acceptance criteria. <ul style="list-style-type: none"> <li>• SPC: PASS; SPC has a Ct within the valid range.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>
<b>INVALID</b>	Presence or absence of the HIV-1 target nucleic acids cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure. <ul style="list-style-type: none"> <li>• SPC: FAIL; SPC Ct is not within valid range.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>
<b>ERROR</b>	Presence or absence of HIV-1 target nucleic acids cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure. <ul style="list-style-type: none"> <li>• HIV-1: NO RESULT</li> <li>• SPC: NO RESULT</li> <li>• Probe Check: FAIL*; all or one of the probe check results fail.</li> </ul> <p>*If the probe check passed, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure.</p>
<b>NO RESULT</b>	Presence or absence of HIV-1 target nucleic acids cannot be determined. Repeat test according to the instructions 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. <ul style="list-style-type: none"> <li>• HIV-1: NO RESULT</li> <li>• SPC: NO RESULT</li> <li>• Probe Check: NA (not applicable).</li> </ul>

**Note** Assay screenshots are for example only. Assay name and version number may vary from the screenshots shown in this package insert. QC1 and QC2 in legends of Figure 5 and Figure 6 control for presence of probes (see Probe Check Control in Section 14, Quality Control); amplification curves are not generated.

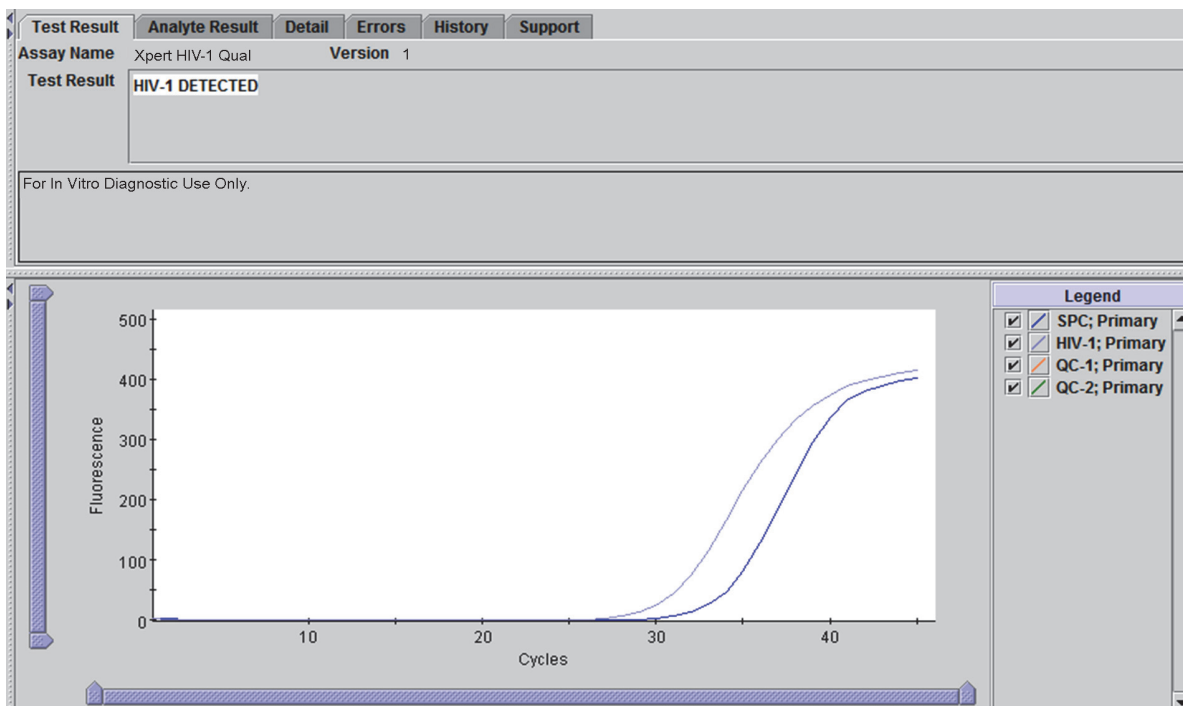


Figure 5. HIV-1 Detected

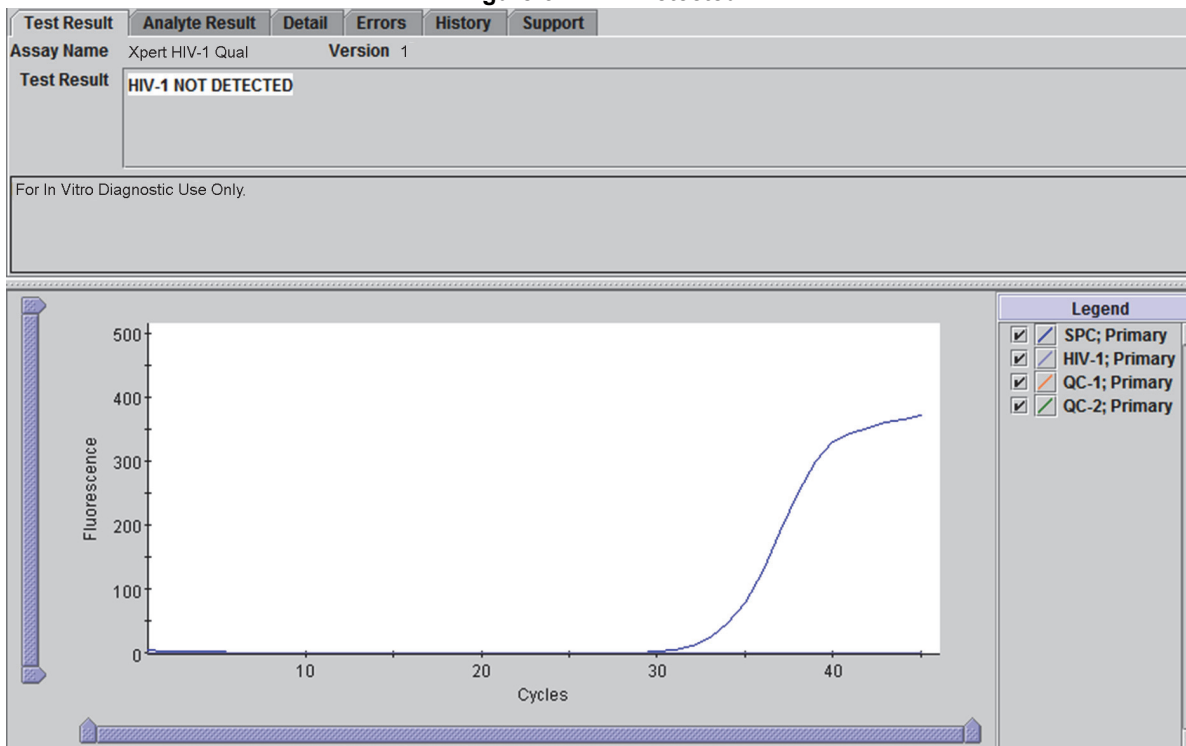


Figure 6. HIV-1 Not Detected

## 16 Retests

### 16.1 Reasons to Repeat the Test

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

- An **INVALID** result indicates one or more of the following:
  - The control SPC failed.
  - The sample was not properly processed or PCR was inhibited.
- An **ERROR** result indicates that the assay 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

For retest of a **NO RESULT**, **INVALID**, or **ERROR** result, use a new cartridge (do not re-use the cartridge) and new reagents.

1. Remove a new cartridge from the kit.
2. See Section 12, Procedure, including Section 12.1, Preparing the Cartridge, and Section 12.2, Starting the Test

## 17 Limitations

- Good laboratory practices and changing gloves between handling specimens are recommended to avoid contamination of reagents.
  1. Rare mutations within the target region of the HIV-1 Qual assay may affect primer and/or probe binding resulting in failure to detect the virus.
  2. A negative test result does not preclude HIV-1 infection. Results from the HIV-1 Qual assay should be interpreted in conjunction with clinical presentation and other laboratory markers.

## 18 Performance Characteristics

### 18.1 Limit of Detection

The limit of detection (LOD) of the HIV-1 Qual assay was determined for both WB and DBS procedures by testing two different HIV-1 subtype B reference standards including the Viral Quality Assurance Laboratory (VQA) reference material of the AIDS Clinical Trials Group and the WHO 3rd International Standard NIBSC code 10/152 diluted in HIV-1 negative EDTA WB. Testing was performed with three dilution series, each analyzed with a unique reagent lot across two operators and three days. In total 72 replicates per level were tested. The evaluation was performed according to CLSI guideline E17-A2.<sup>22</sup> The HIV-1 RNA concentration that can be detected with a positivity rate greater than 95% was determined by Probit regression analysis. The combined results for all three lots tested with both specimens in WB and DBS are shown in Table 2 and Table 3.

**Table 2. Limit of Detection in Whole Blood for the HIV-1 Qual Assay using Probit Regression<sup>a</sup>**

	Nominal Concentration (copies/mL)	No. Replicates	No. Positives	Positivity Rate (%)	LOD with 95% Probability Estimated by Probit (95% Confidence Interval)
VQA	200	72	66	92	203 copies/mL (95% CI: 181-225 copies/mL)
	150	72	55	76	
	100	71	45	63	
	75	72	35	49	
	50	72	34	47	
	25	72	12	17	
	0	72	0	0	
WHO	420	72	72	100	278 copies/mL (95% CI: 253-304 copies/mL)
	300	72	66	92	
	240	72	62	86	
	180	72	57	79	
	120	71	47	66	
	60	72	18	25	
	30	72	13	18	
	0	72	0	0	

a. Conversion factor 1 copy = 1.72 IU used

**Table 3. Limit of Detection in Dried Blood Spots for the HIV-1 Qual Assay using Probit Regression<sup>a</sup>**

	Nominal Concentration (copies/mL)	No. Replicates	No. Positives	Positivity Rate (%)	LOD with 95% Probability Estimated by Probit (95% Confidence Interval)
VQA	800	72	72	100	531 copies/mL (95% CI: 474-587 copies/mL)
	600	71	64	90	
	400	72	64	89	
	200	72	43	60	
	100	72	23	32	
	50	72	4	6	
	0	72	0	0	
WHO	1000	72	71	99	668 copies/mL (95% CI: 593-742 copies/mL)
	750	72	69	96	
	500	72	60	83	
	250	72	43	60	
	125	72	22	31	
	75	72	12	17	
	0	72	0	0	

a. Conversion factor 1 copy = 1.72 IU used



**18.2 Precision**

The precision of the HIV-1 Qual assay was determined for both WB and DBS specimens using four serial dilution panels prepared each with two different HIV-1 subtype B reference standards: the Viral Quality Assurance Laboratory (VQA) reference material of the AIDS Clinical Trials Group and the WHO 3rd International Standard NIBSC code 10/152. Each panel was prepared by spiking the reference standard into HIV-1 negative EDTA WB. Each panel contained an HIV-1 negative WB or DBS panel member. The dried blood spots were prepared by spotting the spiked WB on the filter paper cards with 65 µL and dried prior to testing. The WB and DBS panels were tested per the HIV-1 Qual assay procedure. Each panel member was tested in replicates of four by two operators over nine days. Three different kit lots were used.

The data were analyzed by calculating the percent hit rate for each panel member for each kit lot by specimen type. The HIV-1 Qual assay demonstrates consistent performance at and above the LOD for both WB and DBS specimens as demonstrated by the p-values at >0.05 using the Chi-square statistic. See Table 4 and Table 5.

**Table 4. Precision of HIV-1 Qual Assay in DBS Specimens**

<b>DBS – VQA Reference Standard</b>				
<b>Nominal Concentration HIV-1 RNA copies/mL</b>	<b>Hit Rate (%) (No. pos/No. replicates)</b>			<b>p-value</b>
	<b>Lot 1</b>	<b>Lot 2</b>	<b>Lot 3</b>	
800	100 (24/24)	100 (24/24)	100 (24/24)	1.00
600	92 (22/24)	96 (22/23)	83 (20/24)	0.35
400	92 (22/24)	83 (20/24)	92 (22/24)	0.57
<b>DBS – WHO Reference Standard</b>				
<b>Nominal Concentration HIV-1 RNA copies/mL</b>	<b>Hit Rate (%) (No. pos/No. replicates)</b>			<b>p-value</b>
	<b>Lot 1</b>	<b>Lot 2</b>	<b>Lot 3</b>	
1000	100 (24/24)	96 (23/24)	100 (24/24)	0.36
750	92 (22/24)	96 (23/24)	100 (24/24)	0.35
500	88 (21/24)	71 (17/24)	92 (22/24)	0.12

**Table 5. Precision of HIV-1 Qual Assay in WB Specimens**

<b>WB – VQA Reference Standard</b>				
<b>Nominal Concentration HIV-1 RNA copies/mL</b>	<b>Hit Rate (%) (No. pos/No. replicates)</b>			<b>p-value</b>
	<b>Lot 1</b>	<b>Lot 2</b>	<b>Lot 3</b>	
200	88 (21/24)	96 (23/24)	92 (22/24)	0.58
150	88 (21/24)	79 (19/24)	63 (15/24)	0.12
<b>WB – WHO Reference Standard</b>				

Table 5. Precision of HIV-1 Qual Assay in WB Specimens

WB – VQA Reference Standard				
Nominal Concentration HIV-1 RNA copies/mL	Hit Rate (%) (No. pos/No. replicates)			p-value
	Lot 1	Lot 2	Lot 3	
420	100 (24/24)	100 (24/24)	100 (24/24)	1.00
300	92 (22/24)	100 (24/24)	83 (20/24)	0.11
240	79 (19/24)	83 (20/24)	96 (23/24)	0.22

### 18.3 Linear Range

The linearity of the HIV-1 Qual assay was determined for both the WB and DBS procedures by analysis of a five member panel prepared with serial dilutions of HIV-1 subtype B RNA in HIV-1 negative WB. HIV-1 concentrations ranged from  $1 \times 10^3$  to  $1 \times 10^7$  copies/mL for WB and from  $2.5 \times 10^3$  to  $2.5 \times 10^7$  copies/mL for DBS and each panel member was analyzed in replicates of six using one reagent lot. The reference material used was Acrometrix HIV-1 control. Results for WB and DBS are shown in Figure 7 and Figure 8, respectively, and demonstrate that the assay is linear within a range of  $1 \times 10^3$  to  $1 \times 10^7$  copies/mL with an  $R^2$  value (which is the product of a standard curve) of 0.9931 for WB and within a range  $2.5 \times 10^3$  to  $2.5 \times 10^7$  copies/mL with an  $R^2$  value of 0.9955 for DBS.

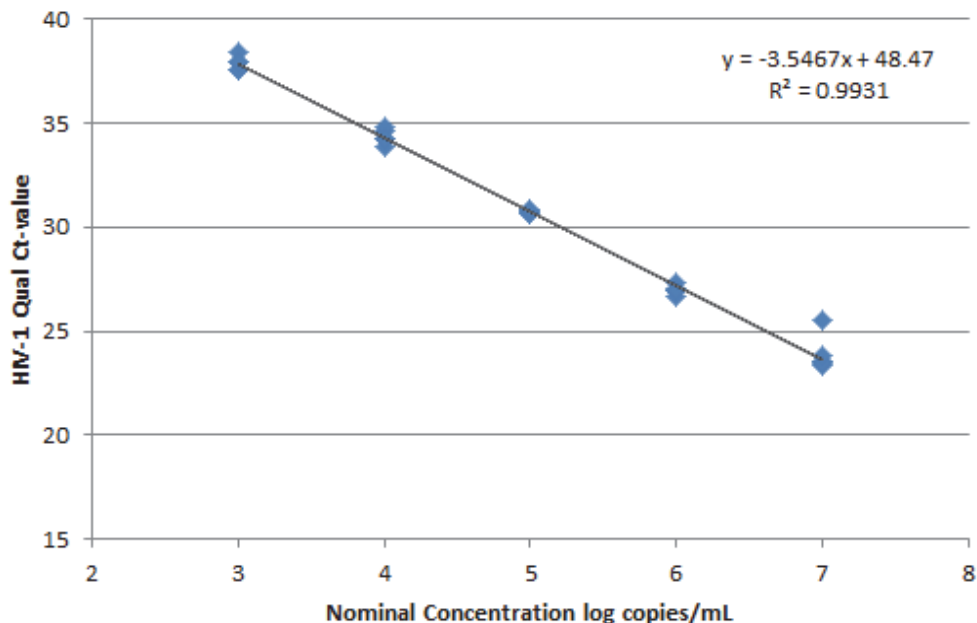


Figure 7. Linearity in Whole Blood for the HIV-1 Qual Assay

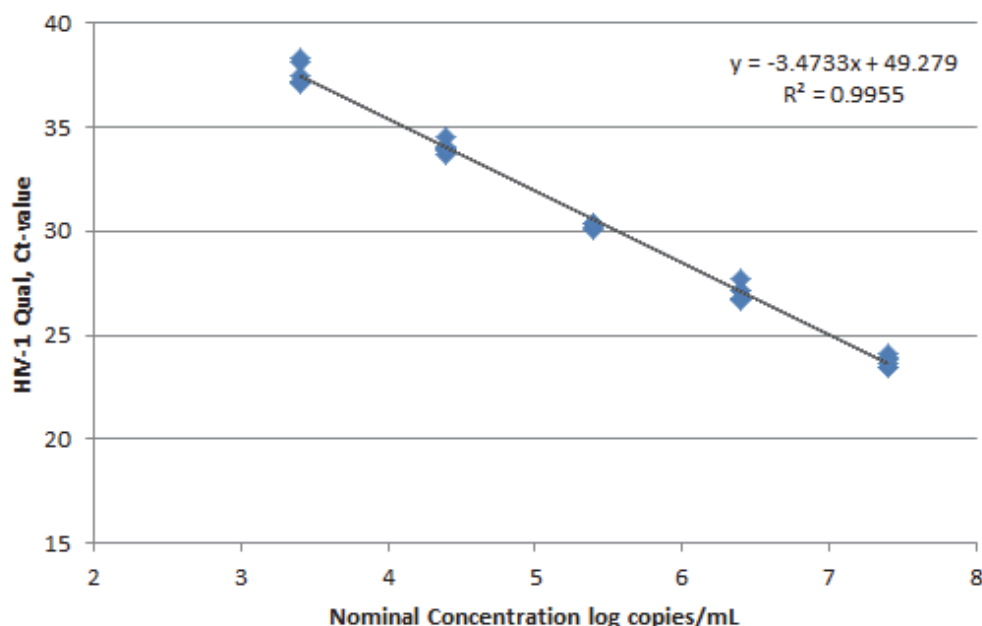


Figure 8. Linearity in Dried Blood Spots for the HIV-1 Qual Assay

**18.4 Analytical Reactivity (Inclusivity)**

The analytical reactivity of the HIV-1 Qual assay was evaluated by testing thirteen isolates representing the HIV-1 Group M subtypes A, C, D, F, G, H, CRF AG/GH, A/E and A/B, Group N, and Group O. The assignment of the nominal stock concentration was performed by Abbott HIV-1 RealTime RT-PCR assay (a polymerase chain reaction). Dilution series consisting of at least six levels cell culture supernatants in HIV-1 negative EDTA WB were made and the limit of detection (LOD) was determined. Each level was tested in replicates of twenty using two reagent lots and the WB procedure. The HIV-1 RNA concentration that can be detected with a positivity rate greater than 95% was determined by Probit regression analysis for each isolate. The determined LOD was verified with the same isolate in replicates of twenty on a third unique reagent lot and with a second isolate of the same group/subtype in replicates of twenty on one reagent lot. Additionally verification was done with one isolate in replicates of 10-20 with one reagent lot using the DBS procedure and the estimated DBS LOD level. The results for LOD and verifications with WB and DBS procedure are summarized in Table 6 and show that the HIV-1 Qual assay detects HIV-1 RNA for thirteen different group/subtypes at concentrations of 680 copies/mL (or lower) for WB and 1400 copies/mL (or lower) for DBS with 95% positivity rate.

Table 6. Analytical Reactivity (Inclusivity) for the HIV-1 Qual Assay

Group/ Subtype	LOD in Whole Blood, 2 Reagent Lots			Verification of LOD in Whole Blood, 3rd Unique Reagent Lot (680 copies/mL)	Verification of LOD with 2nd Isolate in Whole Blood, 1 Reagent Lot (680 copies/mL)		Verification of Recognition with DBS, 1 Reagent Lot (1400 copies/mL)	
	Isolate Designation	LOD (copies/mL)	95% CI	Positivity Rate (%) (n=20)	Isolate Designation	Positivity Rate (%) (n=20)	Isolate Designation	Positivity Rate (%) (n=10-20)
Group M/ Subtype A	92UG029	553	427-678	100	UG275	100	92UG029	100
Group M/ Subtype C	98TZ017	159	117-201	100	92BR025	100	92BR025	100
Group M/ Subtype D	94UG114	379	286-471	100	92UG035	100	92UG035	100

Table 6. Analytical Reactivity (Inclusivity) for the HIV-1 Qual Assay

Group/ Subtype	LOD in Whole Blood, 2 Reagent Lots			Verification of LOD in Whole Blood, 3rd Unique Reagent Lot (680 copies/mL)	Verification of LOD with 2nd Isolate in Whole Blood, 1 Reagent Lot (680 copies/mL)	Verification of Recognition with DBS, 1 Reagent Lot (1400 copies/mL)		
	Isolate Designation	LOD (copies/mL)	95% CI	Positivity Rate (%) (n=20)	Isolate Designation	Positivity Rate (%) (n=20)	Isolate Designation	Positivity Rate (%) (n=10-20)
Group M/ Subtype F	93BR020	262	204-320	100	BZ126	100	93BR020	100
Group M/ Subtype G	RU570	345	267-423	100	BCF-DIOUM	100	RU570	100
Group M/ Subtype H	V1557	171	139-237	100	BCF-KITA	100	V1557	100
Group M/ Subtype J	Clinical Specimen	438	348-527	100	Clinical Specimen	100	Clinical Specimen	100
Group M/ Subtype K	WWRB305-16	550	433-667	100	NA	ND	WWRB305- 16	94.4
Group M/ Subtype CRF A/B	WWRB305-11	208	153-263	100	WWRB305- 12	100	WWRB305- 11	100
Group M/ Subtype CRF A/E	92TH001	228	172-285	100	92TH022	95.0	92TH022	100
Group M/ Subtype CRF AG/ GH	V1525	501	399-603	100	01CM.0008 BBY (A-G)	100	01CM.0008 BBY	100
Group N	YBF30	232	187-277	100	N1FR2011	100	YBF30	100
Group O	MVP5180	189	145-234	100	CA-9	100	MVP5180	100

### 18.5 Analytical Specificity (Exclusivity)

The analytical specificity of the HIV-1 Qual assay was evaluated by adding cultured organisms at  $5 \times 10^3$  particles or copies/mL into HIV-1 negative EDTA WB and into HIV-1 positive EDTA WB at 900 copies/mL HIV-1 reference material (subtype B). Organisms were tested using the WB procedure. Tested organisms are listed in Table 7. None of the organisms tested showed cross reactivity or interference with the HIV-1 detection.

Table 7. Analytical Specificity Organisms

<i>Candida albicans</i>
Cytomegalovirus
Epstein-Barr virus
Hepatitis A virus
Hepatitis B virus
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 A
<i>Staphylococcus aureus</i>

### 18.6 Potentially Interfering Substances

The susceptibility of the HIV-1 Qual assay to interference by elevated levels of endogenous substances and autoimmune disease markers was evaluated. For endogenous substances HIV-1 negative EDTA WB and HIV-1 positive EDTA WB at 2000 copies/mL HIV-1 reference material (subtype B) spiked with the substances were tested.

HIV-1 positive and negative samples with endogenous substances were prepared as DBS and further tested. Elevated levels of the endogenous substances listed in Table 8 were shown to not impact the assay specificity or interfere with the HIV-1 detection.

**Table 8. Endogenous Substances and Concentration Tested**

Substance	Tested Concentration
Albumin (BSA)	90 mg/mL
Bilirubin	0.2 mg/mL
Hemoglobin	5 mg/mL
Human DNA	4 µg/mL
Triglycerides	30 mg/mL

Testing of plasma specimens from five individuals per autoimmune disease marker with and without spiked HIV-1 reference material (subtype B) at 900 copies/mL was done using the WB procedure. No interference with the autoimmune disease markers systemic lupus erythematosus (SLE), anti-nuclear antibodies (ANA) or rheumatoid factor (RF) using the HIV-1 Qual assay were shown.

### 18.7 Seroconversion Sensitivity

The diagnostic sensitivity of the HIV-1 Qual assay was evaluated by testing sequential plasma specimens from fifteen seroconversion panels using the WB procedure. Equivalence of WB and plasma as sample matrix has been proven (see Section 18.8). The HIV-1 Qual assay detected HIV-1 in 52 out of 79 total number of samples compared with 10 out of 79 that were detected by an HIV-1 antibody test (Abbott HIV 1/2 EIA, Abbott PRISM HIV-1/2, Abbott DiaSorin Murex HIV 1.2.O HIV, Bio-Rad GS HIV-1/HIV-2 Plus O EIA, or Siemens HIV 1/O/2 Enhanced ADVIA Centaur). A positive HIV-1 test result in HIV-1 Qual assay was generated earlier in all fifteen panels as compared to the HIV-1 antibody screening. In addition, the first HIV-1 positive response occurred earlier in twelve of the fifteen panels with the HIV-1 Qual assay as compared to the p24 antigen tests (Abbott, Coulter HIV-1 p24 Antigen, Innogenetics RL29, or Perkin Elmer Alliance HIV-1 p24 ELISA). The seroconversion sensitivity is presented in Table 9.

**Table 9. Seroconversion Sensitivity for the HIV-1 Qual Assay**

Old Panel Part Code	Number of Members	Days Spanned	No. of Reactive Panel Members		Days to First Reactive Result		Days between First Reactive Result with HIV-1 Qual and any AB test <sup>a</sup>
			HIV-1 Qual	Antibody (AB) test <sup>a</sup>	HIV-1 Qual	Antibody (AB) test <sup>a</sup>	
PRB946-00-1.0	4	11	3	0	4	11 <sup>c</sup>	7
PRB948-00-1.0	4	23	2	0	20	23 <sup>c</sup>	3
PRB950-00-1.0	4	28	3	1	18	28	10
PRB955-1.0	5	14	5	2	0 <sup>b</sup>	12	12
PRB956-1.0	5	50	4	1	40	50	10
PRB962-1.0	6	17	4	0	7	17 <sup>c</sup>	10
PRB963-1.0	7	21	3	0	14	21 <sup>c</sup>	7
PRB964-1.0	6	22	3	0	15	22 <sup>c</sup>	7
PRB966-1.0	10	51	5	2	35	48	13
PRB973-1.0	4	11	4	1	0 <sup>b</sup>	11	11
PRB974-1.2	4	16	3	1	7	16	9

**Table 9. Seroconversion Sensitivity for the HIV-1 Qual Assay**

Old Panel Part Code	Number of Members	Days Spanned	No. of Reactive Panel Members		Days to First Reactive Result		Days between First Reactive Result with HIV-1 Qual and any AB test <sup>a</sup>
			HIV-1 Qual	Antibody (AB) test <sup>a</sup>	HIV-1 Qual	Antibody (AB) test <sup>a</sup>	
PRB975-1.0	5	14	3	0	7	14 <sup>c</sup>	14
PRB976-1.2	4	9	4	0	0 <sup>b</sup>	9 <sup>c</sup>	9
PRB977-1.0	4	15	3	2	2	13	11
PRB978-1.0	7	33	3	0	26	33 <sup>c</sup>	7
<b>Total</b>	<b>79</b>		<b>52</b>	<b>10</b>			

- a. Antibody tests, based on vendor data: Abbott HIV 1/2 EIA, Abbott PRISM HIV-1/2, Abbott Murex HIV 1.2.O HIV, Bio-Rad GS HIV-1/HIV-2 Plus O EIA, Siemens HIB 1/O/2 Enhanced ADVIA Centaur
- b. All bleed results were detected with the HIV Qual assay
- c. All bleeds were non-reactive for HIV-1 Antibodies (based on vendor information). The last bleed day is used as "Days to First Reactive Result"

### 18.8 Sample Type Equivalence (Whole Blood and Plasma)

The equivalent performance for the two different sample types EDTA WB and EDTA plasma using the HIV-1 Qual assay was demonstrated with specimens from sixteen HIV-1 negative individuals. Each specimen was split and prepared in one plasma aliquot and one WB aliquot. Both aliquots were spiked with HIV-1 RNA at 700 copies/mL. The aliquots were analyzed side-by-side using the WB protocol. Equivalent performance between the sample types was shown.

## 19 Clinical Performance

Performance characteristics of the HIV-1 Qual assay were evaluated at two institutions in Africa.

Subjects included individuals whose routine care called for collection of WB or DBS specimens for HIV-1 testing. For eligible subjects, aliquots of leftover specimens were obtained for testing with the HIV-1 Qual assay and comparator testing. Patient management continued at the site per their standard practice independent of the investigational test results.

The HIV-1 Qual assay performance was compared to a CE-marked comparator assay. The comparator assay was validated for DBS and not for WB therefore HIV-1 Qual WB assay results were compared to DBS results of the comparator method. Repeat testing on both the HIV-1 Qual assay and the comparator assay was performed on specimens where the HIV-1 Qual assay and the comparator assay were discrepant, and is provided for informational purposes only.

### 19.1 Results of WB Specimens

A total of 106 WB specimens were tested for HIV-1 by the HIV-1 Qual assay and the comparator assay. The HIV-1 Qual assay demonstrated positive percent agreement (PPA) of 98.2% (95% CI 90.3-100), and negative percent agreement (NPA) of 98.0% (95% CI 89.6-100), on WB relative to the comparator assay. Results are shown in Table 10.

**Table 10. HIV-1 Qual Assay Performance vs. Comparator Assay – WB Specimens**

		Comparator HIV-1 Qual Assay – DBS		
		POS	NEG	Total
HIV-1 Qual Assay WB	POS	54	1 <sup>a</sup>	55
	NEG	1 <sup>b</sup>	50	51
	Total	55	51	106
		PPA:	98.2% (95% CI: 90.3-100)	
		NPA:	98.0% (95% CI: 89.6-100)	

- a. Upon retesting, specimen was Xpert POS / comparator POS
- b. Upon retesting, specimen was Xpert NEG / comparator POS

**19.2 Results of DBS Specimens**

A total of 399 DBS specimens were tested for HIV-1 by the HIV-1 Qual assay and the comparator assay. The HIV-1 Qual assay demonstrated a sensitivity with PPA of 95.6% (95% CI 91.8-98.0), and specificity with NPA of 98.5% (95% CI 95.6-99.7), on DBS relative to the comparator assay. Results are shown in Table 11.

**19.3 Specificity in HIV Sero-Negative Adult Blood Donors****Table 11. HIV-1 Qual Assay Performance vs. Comparator Assay – DBS Specimens**

		Comparator HIV-1 Qual Assay		
		POS	NEG	Total
HIV-1 Qual Assay	POS	194	3 <sup>a</sup>	197
	NEG	9 <sup>b</sup>	193	202
	Total	203	196	399
		PPA:	95.6% (95% CI: 91.8-98)	
		NPA:	98.5% (95% CI: 95.6-99.7)	

- a. Upon retesting, 1 of 3 specimens was Xpert NEG / comparator NEG, and 2 of 3 specimens were Xpert POS / comparator POS
- b. Upon retesting, 5 of 9 specimens were Xpert POS / comparator POS, 3 of 9 specimens were Xpert NEG / comparator POS, and 1 of 9 was Xpert NEG / comparator NEG.

WB collected in EDTA was collected from 1017 blood donors at two sites in the United States. The specimens were determined to be HIV-1 negative by standard blood bank FDA-licensed antibody and nucleic acid methods. Of the 1017 specimens 503 were prepared as DBS and 514 were tested as WB by the HIV-1 Qual assay. One DBS and two WB specimens were indeterminate on both initial and retest, and therefore excluded from the specificity calculation. The specificity of the assay was 100% (1014/1014), 95% CI: 99.6-100.0).

**19.4 Assay Success Rate**

Of the HIV-1 Qual assay runs performed with eligible specimens, 97.0% (1483/1529) of these specimens were successful on the first attempt. The remaining 46 gave indeterminate results on the first attempt. Of the 46 indeterminate cases, 36 yielded valid results upon repeat assay; three were indeterminate upon retest and seven of the indeterminate cases were not repeated due to insufficient remaining volume. The overall rate of assay success was 99.3% (1519/1529).

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## 22 Technical Assistance

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## 23 Table of Symbols

Symbol	Meaning
	Catalog number
	<i>In vitro</i> diagnostic medical device
	Do not reuse
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <n> tests
	Control
	Expiration date
	CE marking – European Conformity
	Temperature limitation
	Biological risks



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