

## WHO Prequalification of In Vitro Diagnostics PUBLIC REPORT

**Product: Xpert® HCV Viral Load with GeneXpert® Dx,  
GeneXpert® Infinity-48s, and GeneXpert® Infinity-80  
WHO reference number: PQDx 0260-070-00**

**Xpert® HCV Viral Load with GeneXpert® Dx, GeneXpert® Infinity-48s, and GeneXpert® Infinity-80** manufactured by **Cepheid AB, CE marked**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 04 April 2017.

### **Intended use:**

Xpert® HCV Viral Load, performed on GeneXpert® Instrument Systems is designed for the quantitation of hepatitis C virus (HCV) RNA in human serum or plasma (EDTA) from HCV-infected individuals. The test utilizes automated reverse transcriptase polymerase chain reaction (RT-PCR) using fluorescence to detect the RNA of interest for the quantitation of HCV.

Xpert® HCV Viral Load quantifies HCV genotypes 1–6 over the range of 10 to 100,000,000 IU/mL. Xpert® HCV Viral Load is intended for use as an aid in the management of HCV infected patients undergoing antiviral therapy. The test measures HCV RNA levels at baseline and during treatment and can be utilized to predict sustained and non-sustained virological responses to antiviral therapy.

Results from Xpert® HCV Viral Load may also be used to confirm HCV infection in anti-HCV positive individuals. In anti-HCV positive individuals who test negative for HCV RNA, use of another anti-HCV serological assay may be considered for distinction between true HCV exposure and biologic false positivity. Repeat HCV RNA testing may be indicated in cases that have had HCV exposure in the last 6 months or have clinical evidence of HCV disease.

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

### **Assay description:**

GeneXpert® Instrument Systems automate and integrate specimen purification, nucleic acid amplification, and detection of the target sequence in simple or complex specimens using real-time reverse transcriptase PCR (RT-PCR) which uses fluorescence to detect the RNA of interest. The systems consist of an instrument, personal computer, and preloaded software for running 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*.

Xpert® HCV Viral Load includes reagents for the detection of HCV RNA in specimens as well as two internal controls used for quantitation of HCV RNA. The internal controls monitor recovery and 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.

**Test kit contents:**

<b>Xpert® HCV Viral Load</b>	<b>10 tests (product code GXHCV-VL-CE-10)</b>
Xpert® HCV Viral Load cartridges with integrated reaction tubes	10
Disposable 1 mL transfer pipettes	1 bag of 10 per kit
CD (includes instructions for use)	1

**Instrumentation:**

<b>Product name</b>	<b>Product code</b>
GeneXpert® Dx (including barcode scanner and operator manual)	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
GeneXpert® Infinity-48s (including barcode scanner and operator manual)	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
GeneXpert® Infinity-80 (including barcode scanner and operator manual)	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
GeneXpert Dx Software Version 4.6a or higher (GeneXpert Dx systems); or Xpertise 6.2a or higher (Infinity-80/Infinity-48s)	GX4.OSWKIT, XPERTISE-G2-SWKIT

**Items required but not provided:**

<b>Item</b>
<b>Consumables:</b> Bleach or sodium hypochlorite 70% Ethanol Disposable gloves (one for each specimen processed)

K2-EDTA specimen tubes EDTA Plasma Preparation Tubes (PPT) Serum collection tubes
<b>Equipment:</b> Printer (see Cepheid representative for additional information) Centrifuge for processing serum and plasma specimens

**Storage:**

The test kit (Xpert® HCV Viral Load) should be stored at 2 to 28 °C.

**Shelf-life upon manufacture:**

12 months.

**Warnings/limitations:**

Xpert® HCV Viral Load is not intended to be used as a donor screening test for HCV.

The cartridge contains guanidinium thiocyanate as the lysis reagent. This chemical is highly toxic and all care should be taken when using the cartridges in case of spills etc. Please note that as this chemical is also highly toxic to aquatic life, it should optimally be disposed of by incineration. No liquids from the cartridge should be released into the environment.

WHO made a number of suggested changes to the instructions for use, these will be implemented with the next version update (expected quarter 3 2017).

**Summary of WHO prequalification assessment for Xpert® HCV Viral Load**

	Date	Outcome
<b>PQ listing</b>	04 April 2017	listed
<b>Dossier review</b>	N/A	MR
<b>Site inspection(s) of quality management system</b>	23 to 25 June 2015	MR
<b>Laboratory evaluation of performance and operational characteristics</b>	2 March 2017	MR

MR: Meets requirements

N/A: Not applicable

**Prioritization for prequalification**

Based on the established criteria, Xpert® HCV Viral Load was given priority for WHO prequalification.

**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® HCV Viral Load as per the "Instructions for compilation of a product dossier" (PQDx\_018 v1). Notwithstanding, certain aspects of the product dossier previously submitted for stringent regulatory review were reviewed by an assessor during the site inspection.

Commitments for prequalification:

1. The manufacturer will undertake a field based performance study in the sub Saharan African region with intended users by June 2017.
2. The instructions for use will be updated with information defining the minimal qualifications or training requirements for the intended user (laboratory personnel with minimal training) based on the outcome of this study.

WHO will follow-up on implementation of these commitments at the next inspection.

### **Manufacturing site inspection**

In accordance with the WHO procedure for abbreviated prequalification assessment, a shortened inspection with fewer inspectors was conducted at the site(s) of manufacture Röntgenvägen 5, SE-171 54 Solna, Sweden of Xpert® HCV Viral Load between 23 and 25 June 2015<sup>1</sup> as per the “Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics” (PQDx\_014 v1).

The inspection 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 23 May 2016.

Based on the site inspection and corrective action plan review, the quality management system for Xpert® HCV Viral Load with GeneXpert Dx, GeneXpert Infinity-48, GeneXpert Infinity-48s and GeneXpert Infinity-80 meets WHO prequalification requirements.

### **Laboratory evaluation**

Xpert® HCV Viral Load is intended for use in human EDTA plasma /serum specimens. A volume of 1000µl of specimen is needed to perform the assay. This type of assay requires general laboratory equipment such as centrifuge, vortex as well as continuous electricity and cannot be performed in laboratories with limited facilities.

The limit of detection (LOD) of the assay was confirmed at 4.91 IU/mL (95% CI: 3.17 to 10.69 IU/mL) using the 5th WHO International Standard for HCV NAT (NIBSC code: 14/150).

All genotypes present in the 4th HCV RNA Genotype Panel for Nucleic Acid Amplification (NIBSC code: 14/290) were detected. Fourteen of the 15 specimens in the NRL HCV RNA Mixed Genotype Panel were detected; one specimen (Genotype 2) was invalid on initial and repeat testing.

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<sup>1</sup> Sites at 904 Caribbean Drive, Sunnyvale 94089-1189, California, USA and 1339 Moffet Park Drive, Sunnyvale 94089, California, USA were also inspected on 29 to 30 June 2015.

In this limited performance evaluation on a panel of 102 clinical specimens, we found an initial bias (95% CI) of -0.135 (-0.1839 to -0.0859) compared to the reference results. The sensitivity (95% CI) was 100% (94.6% to 99.9%) and a specificity (95% CI) of 100% (75.9 % to 99.4%) compared to the reference results.

In this study, the invalid rate was 0.48% and the error rate was 1.67%.

<b>Performance characteristics in comparison with an agreed reference standard</b>	
	<b>Initial estimate (95% CI)</b>
<b>Sensitivity %</b>	100% (94.6 to 99.9%)
<b>Specificity %</b>	100% (75.9 to 99.4%)
<b>Invalid rate %</b>	0.48%
<b>Error rate %</b>	1.67%

<b>Additional performance characteristics</b>	
<b>Genotype detection</b>	All genotypes present in the 4th HCV RNA Genotype Panel for Nucleic Acid Amplification (NIBSC code: 14/290) were detected. 14/15 specimens in the NRL HCV RNA Mixed Genotype Panel were detected.
<b>Limit of detection using 5th WHO International Standard for HCV NAT (NIBSC code: 14/150)</b>	4.91 IU/mL (95% CI: 3.17 to 10.69 IU/mL)
<b>Cross-contamination</b>	0%

<b>Key operational characteristics</b>	
Validated specimen types	EDTA plasma, serum
Number of steps	2
Time to result	1 hour: 45 minutes
Internal QC	Sample Processing Control (SPC): Armored RNA® in the form of a dry bead that 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 maximum 30 minutes after addition of specimen.

## **Labelling**

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

### 1. Labels

(240)GXHCV-VL-CE-10,(10)XXXXXXXXXXXXXXXXXX,(22)1,(17)XXXXXXXXXX,(01)7332940001544

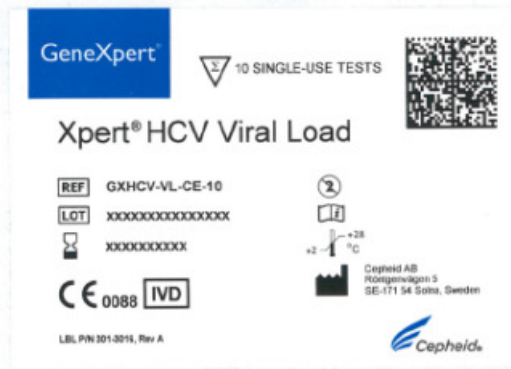


Figure 1: kit carton label

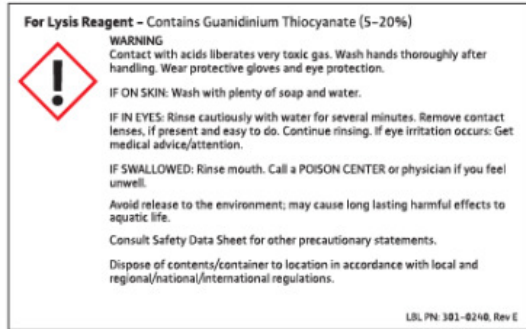
(240)GXHCV-VL-CE-10,(10)XXXXXXXXXXXXXXXXXX,(22)1,(17)XXXXXXXXXX,(01)7332940001544



Figure 2: kit corner label

### Lysis Reagent Guanidinium Thiocyanate Kit Hazard Label

Updated 07/06/15



Stock Label p/n 301-0240, Rev E

Material:	Transtherm 1C Paper
Colors:	Black, PMS 186C Red
Adhesive:	AT20
Topcoat:	Full UV Varnish
Label Size:	4" x 2.50"
Copy Unwind Position:	#4
General Specifications:	Reference Cepheid Doc D7280 for additional requirements

Figure 3: kit hazard label



Figure 4: cartridge label



# Xpert<sup>®</sup> HCV Viral Load

**REF** GXHCV-VL-CE-10

## **Trademark, Patents and Copyright Statements**

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Windows<sup>®</sup> is a trademark of Microsoft Corporation.

Armored RNA<sup>®</sup> is a patented technology jointly developed by Asuragen Inc. and Cenetron Diagnostics, LLC under U.S. Patent Nos. 5,677,124, 5,919,625, 5,939,262 and other patents pending.

THE PURCHASE OF THIS PRODUCT CONVEYS TO THE BUYER THE NON-TRANSFERABLE RIGHT TO USE IT IN ACCORDANCE WITH THIS PACKAGE INSERT. NO OTHER RIGHTS ARE CONVEYED EXPRESSLY, BY IMPLICATION OR BY ESTOPPEL. FURTHERMORE, NO RIGHTS FOR RESALE ARE CONFERRED WITH THE PURCHASE OF THIS PRODUCT.

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# Xpert<sup>®</sup> HCV Viral Load

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For *In Vitro* Diagnostic Use Only.

## 1 Proprietary Name

Xpert<sup>®</sup> HCV Viral Load

## 2 Common or Usual Name

HCV VL

## 3 Intended Use

The HCV VL Assay, performed on GeneXpert<sup>®</sup> Instrument Systems, is designed for the rapid quantitation of Hepatitis C Virus (HCV) RNA in human serum or plasma (EDTA) from HCV-infected individuals. The test utilizes automated reverse transcriptase polymerase chain reaction (RT-PCR) using fluorescence to detect the RNA of interest for the quantitation of HCV.

The HCV VL Assay quantifies HCV genotypes 1–6 over the range of 10 to 100,000,000 IU/mL. The HCV VL Assay is intended for use as an aid in the management of HCV infected patients undergoing antiviral therapy. The test measures HCV RNA levels at baseline and during treatment and can be utilized to predict sustained and nonsustained virological responses to HCV therapy.

Results from the HCV VL Assay may also be used to confirm HCV infection in anti-HCV positive individuals. In anti-HCV positive individuals who test negative for HCV RNA, use of another HCV antibody assay may be considered for distinction between true HCV exposure and biologic false positivity. Repeat HCV RNA testing may be indicated in cases that have had HCV exposure in the last 6 months or have clinical evidence of HCV disease.

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

## 4 Summary and Explanation

HCV is a member of the Flaviviridae family and has been recognized as the major causative agent of chronic liver disease, including chronic active hepatitis, cirrhosis and hepatocellular carcinoma.<sup>1</sup> The HCV genome is a positive-sense RNA molecule of approximately 9500 nucleotides.<sup>1</sup> HCV is usually transmitted through percutaneous exposure to infected blood, primarily by intravenous drug use and receipt of unscreened donated blood products. Less frequently, HCV has been shown to be transmitted through occupational, perinatal and sexual exposures.<sup>2</sup>

An estimated 185 million people, or roughly 3% of the world's population, have been infected with HCV, and over 80% live in Low and Middle Income Countries (LMICs).<sup>3</sup> The burden of disease is greatest in developing countries; the highest reported prevalences are in China (3.2%)<sup>4</sup> Pakistan (4.8%)<sup>4</sup>, Nigeria (18.3%)<sup>5</sup> and Egypt (22%)<sup>4</sup>. About 15 million European adults are infected with HCV and most of these people are unaware of their infection.<sup>6</sup> Each year, 350,000 to 500,000 people die from HCV-related liver disease.<sup>7</sup>

Antiviral medicines can cure HCV, but access to diagnosis and treatment is low.<sup>7</sup> A cure for HCV infection is now possible in most patients with highly effective, safe and tolerable combinations of oral direct-acting antivirals (DAAs) taken for 8–24 weeks.<sup>5</sup> Eradication of HCV is being discussed for the first time.<sup>5</sup>

Quantitation of HCV RNA has proven useful in providing a metric to evaluate the effectiveness of antiviral response to HCV treatment. Guidelines for the management and treatment of HCV recommend quantitative testing for HCV RNA before the start of antiviral therapy, during therapy, and after the conclusion of treatment. The primary objective of treatment is Sustained Virologic Response (SVR), defined as undetectable HCV RNA by a sensitive test 12 or 24 weeks after the end of treatment depending on the anti-HCV therapy.<sup>8</sup>

## 5 Principle of the Procedure

The GeneXpert Instrument Systems automate and integrate sample purification, nucleic acid amplification, and detection of the target sequence in simple or complex samples using RT-PCR which uses fluorescence to detect the RNA of interest. The systems consist of an instrument, personal computer, and preloaded software for running 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 systems, refer to the appropriate *GeneXpert Dx Operator Manual* or *GeneXpert Infinity Operator Manual*.

The HCV VL Assay includes reagents for the detection of HCV RNA in specimens as well as two internal controls used for quantitation of HCV RNA. The internal controls monitor recovery and 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 HCV VL Assay kit contains sufficient reagents to process 10 specimens or quality control samples. The kit contains the following:

<b>HCV VL 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)	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
<b>Disposable 1 mL Transfer Pipettes</b>	<b>10 per kit</b>
<b>CD</b>	<b>1 per kit</b>
• Assay Definition File (ADF)	
• Instructions to import ADF into GeneXpert software	
• Package Insert	

**Note** Safety Data Sheets (SDS) are available at [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 commingling of the material with other animal materials.

## 7 Storage and Handling



- Store the HCV VL Assay cartridges and reagents at 2–28 °C.
- Do not open the cartridge until you are ready to perform the assay.
- Do not use a cartridge that has leaked.
- Do not use HCV VL Assay cartridges and reagents that were previously frozen.
- Do not use reagents or cartridges that have passed the expiration date.

## 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 4.6a or higher (GeneXpert Dx systems); or Xpertise 6.2a 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.
- Bleach or sodium hypochlorite

## 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>9</sup> and the Clinical and Laboratory Standards Institute.<sup>10</sup>
- Good laboratory practices and changing gloves between handling specimens are recommended to avoid contamination of specimens or reagents.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Do not substitute HCV VL Assay reagents with other reagents.
- Do not open the HCV VL Assay cartridge lid except when adding sample.
- 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 use a cartridge that has a damaged reaction tube.
- Do not use a cartridge that has leaked.
- ② • Each single-use HCV VL Assay cartridge is used to process one test. Do not reuse cartridges.
- ② • The single-use disposable pipette is used to transfer one specimen. Do not reuse spent disposable pipettes.
- 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 or controls, thoroughly clean the contaminated area with a solution of 1:10 dilution of household chlorine bleach or sodium hypochlorite and then 70% ethanol or 70% denatured ethanol. Wipe work surfaces dry completely before proceeding.
- Consult your institution's environmental waste personnel on proper disposal of used cartridges and unused reagents. Check state, territorial, or local regulations as they may differ from national disposal regulations. The material may exhibit characteristics of hazardous waste requiring specific disposal requirements. Institutions should check their hazardous waste disposal requirements.

## 10 Chemical Hazards<sup>11,12</sup>



- CLP/GHS Hazard Pictogram:
- Signal Word: Warning
- Hazard Class: Acute toxicity, oral 5, Chronic aquatic toxicity 3, Irritant (eye) 2B, Irritant (skin) 3
- Lysis Reagent contains guanidinium thiocyanate
  - Hazard Statements: H302: Harmful if swallowed, H316: Causes mild skin irritation, H320: Causes eye irritation, H412: Harmful to aquatic life with long lasting effects, EUH031: Contact with acids liberates toxic gas.
- Precautionary Statements:
  - **P264:** Wash hands thoroughly after handling.
  - **P280:** Wear protective gloves/eye protection/face protection.
  - **P273:** Avoid release to the environment.
  - **P302 + P352:** IF ON SKIN: Wash with plenty of soap and water.
  - **P305 + P351 + P338:** IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
  - **P312:** Call a POISON CENTER or physician if you feel unwell.
  - **P510:** Dispose of contents/container to location in accordance with local/regional/national/international regulations.

## 11 Specimen Collection, Storage, and Transport

Whole blood should be collected in K2-EDTA tubes, EDTA-PPT or serum collection tubes and centrifuged to separate the plasma/serum and red blood cells per the manufacturer’s instructions.

### Collection

- A minimum of 1 mL plasma or serum is required for the HCV VL Assay. If using the transfer pipette included in the kit, a minimum of 1.2 mL plasma or serum is required. Alternatively, if using a precision pipette, a minimum of 1 mL plasma or serum is required.
- Whole blood may be held at 15–35 °C for 6 hours, at 15–25 °C for 24 hours or at 2–8 °C for up to 72 hours prior to preparing and analyzing the specimen.
- After centrifugation, plasma and serum may be held at 15–35 °C for 24 hours or at 2–8 °C for three days prior to testing.
- Plasma and serum specimens are stable frozen (-70 to -18 °C) for 6 weeks.
- Plasma and serum specimens are stable for up to three freeze/thaw cycles.
- Plasma and serum specimens must be thawed and equilibrated to room temperature prior to transfer to the cartridge.



### Storage

- Serum and plasma samples may be frozen and thawed up to three times without loss of HCV RNA.

### Transport

- Ship whole blood, plasma or serum specimens at 2–8 °C.
- Transportation of whole blood, plasma or serum specimens must comply with country, federal, state and local regulations for the transportation of etiologic agents.



## 12 Procedure

### 12.1 Preparing the Specimen

1. Following centrifugation of whole blood samples, 1 mL of plasma can be pipetted directly into the cartridge.
2. If using frozen specimens, place the specimens at room temperature (20–35 °C) until completely thawed and equilibrated to room temperature before use.
3. Plasma and serum samples stored in 2–8 °C should be removed from the refrigerator and equilibrated to room temperature before use.
4. Plasma samples stored at 2–8 °C or frozen and thawed should be vortexed for 15 seconds before use, and if specimen is cloudy, clarify by a quick centrifugation.



## 12.2 Preparing the Cartridge

1. Wear protective disposable gloves.
  2. Inspect the test cartridge for damage. If damaged, do not use it.
  3. Open the lid of the test cartridge.
- **Option 1:** If using the transfer pipette included in the kit (Figure 1), fill to just below the bulb but above the line to transfer at least 1 mL plasma or serum from the collection tube into the sample chamber of the test cartridge (Figure 2). Do **NOT** pour the specimen into the chamber!
  - **Option 2:** If using an automatic pipette, transfer at least 1 mL of plasma or serum into the sample chamber of the test cartridge (Figure 2). Do **NOT** pour the specimen into the chamber!

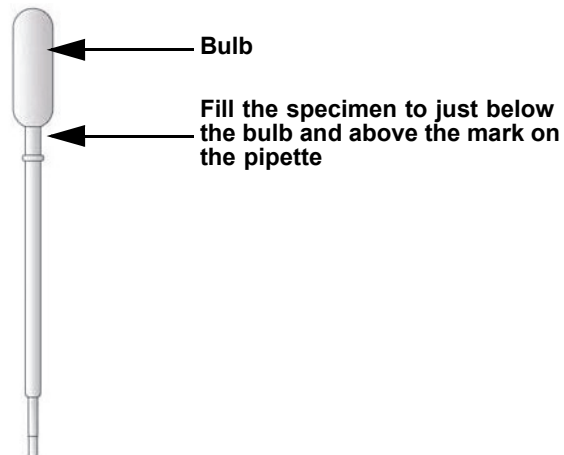


Figure 1. HCV VL Assay Transfer Pipette

4. Close the cartridge lid.
5. Load the cartridge into the GeneXpert Dx instrument or Infinity system.

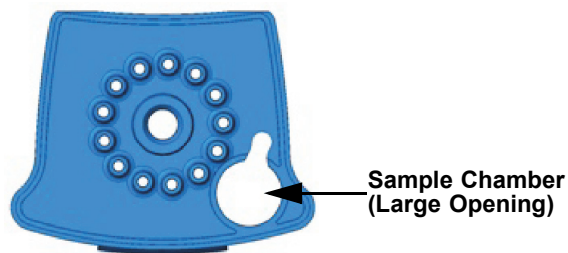


Figure 2. HCV VL Assay Cartridge (Top View)

### 12.3 Starting the Test

**Important** Before you start the test, make sure the HCV VL Assay Definition File (ADF) is imported into the software.

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

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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:
  - 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 GeneXpert 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 **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 HCV VL 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*, depending on the instrument used.

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), Internal Quantitative Standard High and Low (IQS-H and IQS-L, also acts a specimen processing control [SPC]) and Probe Check Control (PCC).

- **Sample Volume Adequacy (SVA)** – Ensures 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 be displayed if there is no sample or an **ERROR 2097** will be displayed if there is not enough sample. The system will prevent the user from resuming the test.
- **Internal Quantitative Standard High and Low (IQS-H and IQS-L)** – IQS-H and IQS-L are two Armored RNA® constructs in the form of a dry bead that goes through the whole assay process. The IQS-H and IQS-L are standards calibrated against the WHO 4th International standard for HCV. They are used for quantification by using lot specific parameters for the calculation of HCV RNA concentration in the sample. Additionally IQS-H and IQS-L detect specimen-associated inhibition of the RT-PCR reaction. The IQS-H and IQS-L pass if they meet 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, not available in the kit, 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 (Figure 3 and Figure 5). Possible results are shown in Table 1.

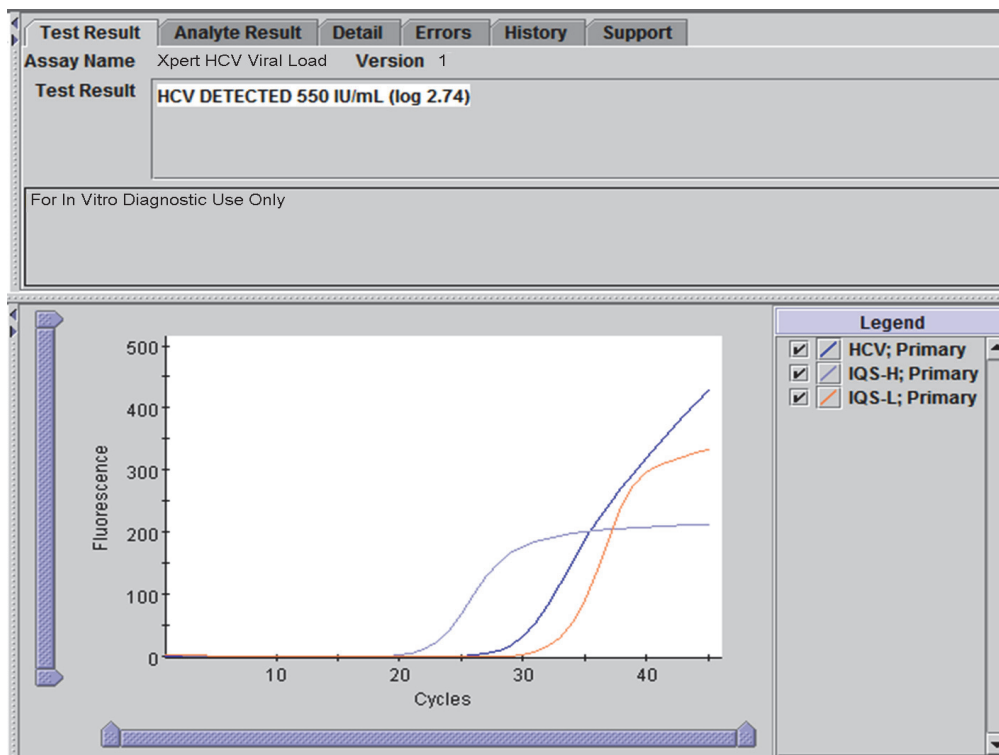
**Table 1. HCV VL Assay Results and Interpretation**

Result	Interpretation
<b>HCV DETECTED</b> <b>XX IU/mL (log X.XX)</b> See Figure 3.	The HCV RNA is detected at XX IU/mL. <ul style="list-style-type: none"> <li>• The HCV RNA has a titer within the linear range setting of the assay and the endpoint above the minimum.</li> <li>• IQS-H and IQS-L: PASS.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>
<b>HCV DETECTED</b> <b>&gt; 1.00E08 IU/mL</b> See Figure 4.	The HCV RNA is detected above the quantitative range of the assay. <ul style="list-style-type: none"> <li>• IQS-H and IQS-L: PASS.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>
<b>HCV DETECTED</b> <b>&lt; 10 IU/mL</b> See Figure 5.	The HCV RNA is detected below the quantitative range of the assay. <ul style="list-style-type: none"> <li>• IQS-H and IQS-L: PASS.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>
<b>HCV NOT DETECTED</b> See Figure 6.	The HCV RNA is not detected. <ul style="list-style-type: none"> <li>• HCV RNA is not detected.</li> <li>• IQS-H and IQS-L: PASS.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>
<b>INVALID</b> See Figure 7.	Presence or absence of the HCV RNA cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure. <ul style="list-style-type: none"> <li>• IQS-H and/or IQS-L: FAIL; Cycle thresholds (Cts) are not within valid range and the endpoint is below the minimum setting.</li> <li>• Probe Check: PASS; all probe check results pass.</li> </ul>

**Table 1. HCV VL Assay Results and Interpretation (Continued)**

Result	Interpretation
<b>ERROR</b> See Figure 8.	<p>Presence or absence of HCV RNA cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure.</p> <ul style="list-style-type: none"> <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>	<p>Presence or absence of HCV RNA cannot be determined. Repeat test according to the instructions in Section 16.2, Retest Procedure. A <b>NO RESULT</b> indicates that insufficient data were collected. For example, the operator stopped a test that was in progress.</p>

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



**Figure 3. HCV Detected and Quantified**

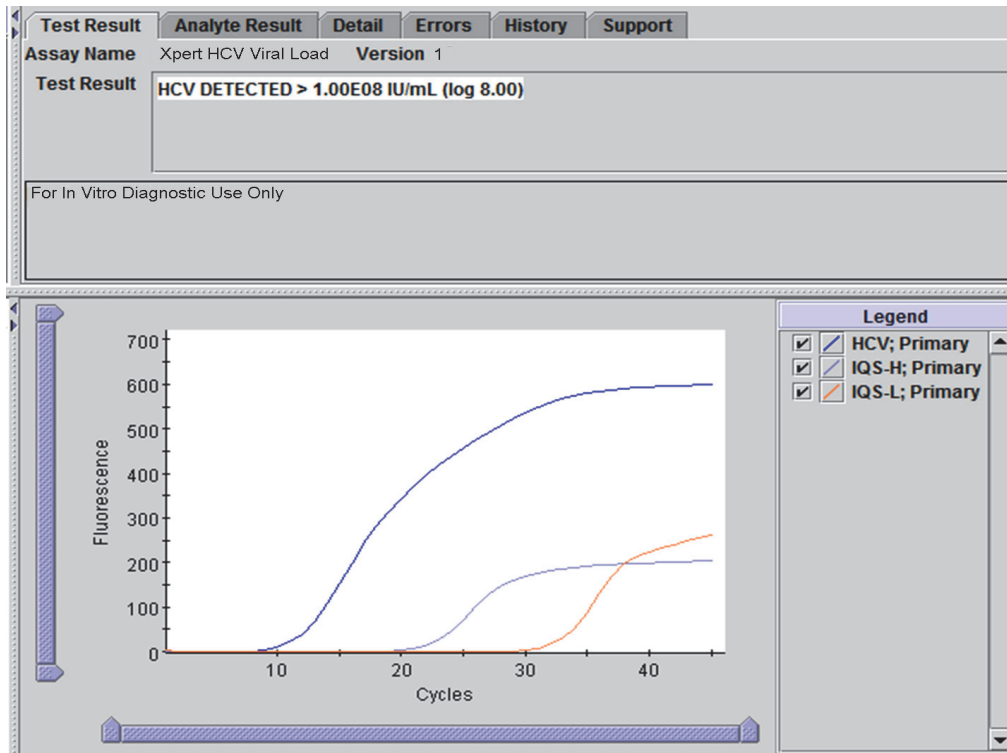


Figure 4. HCV Detected

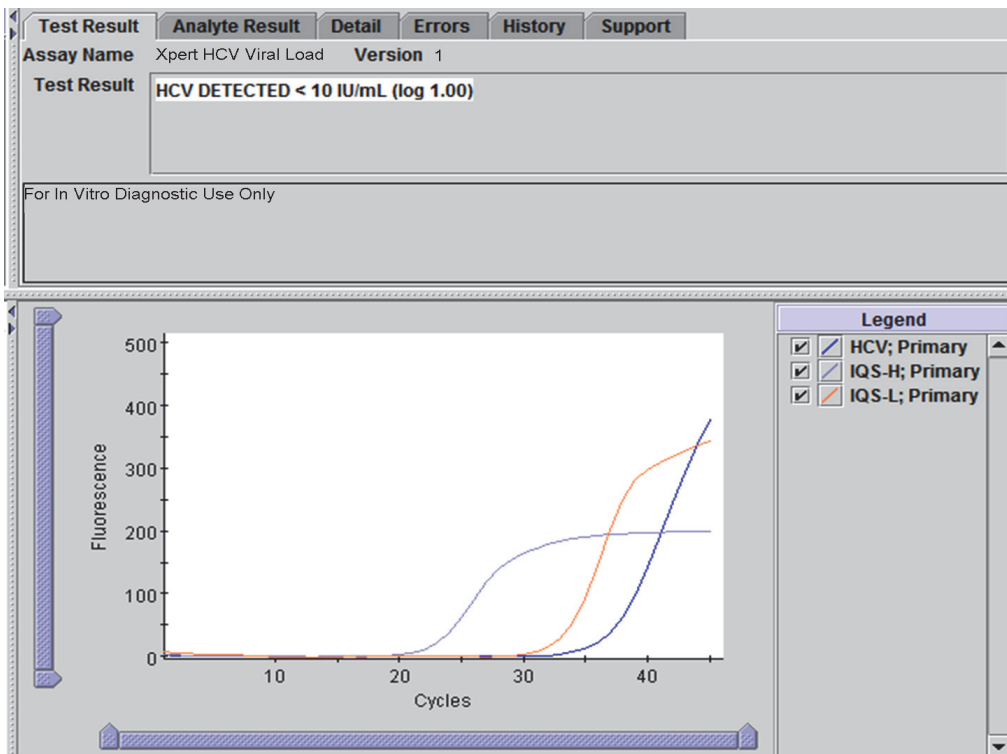


Figure 5. HCV Detected

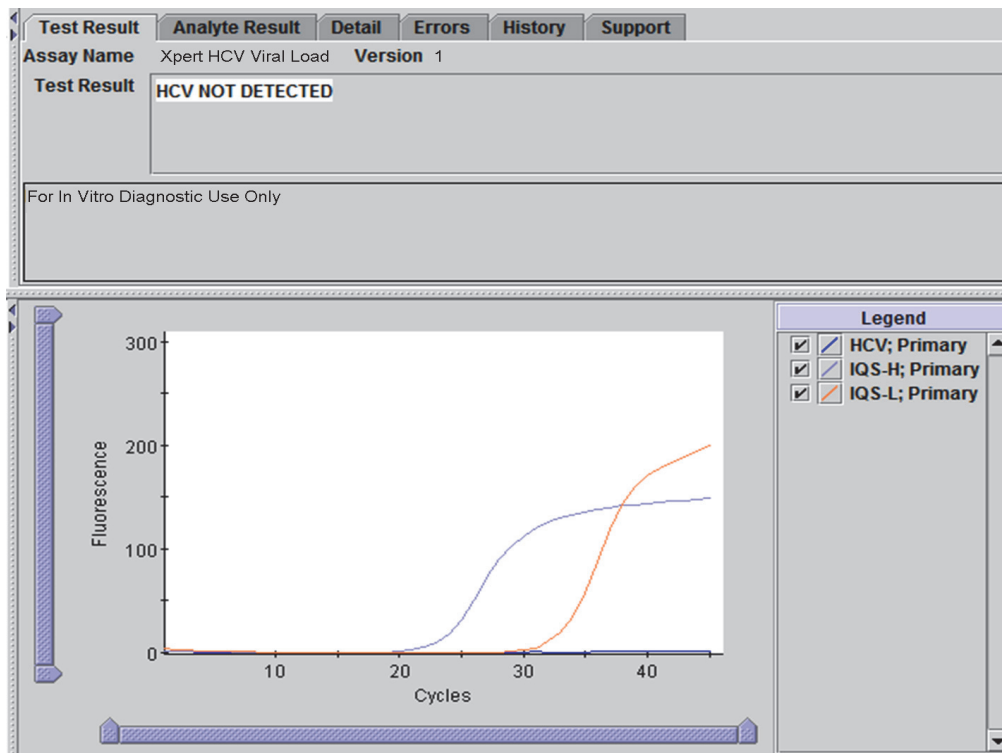


Figure 6. HCV Not Detected

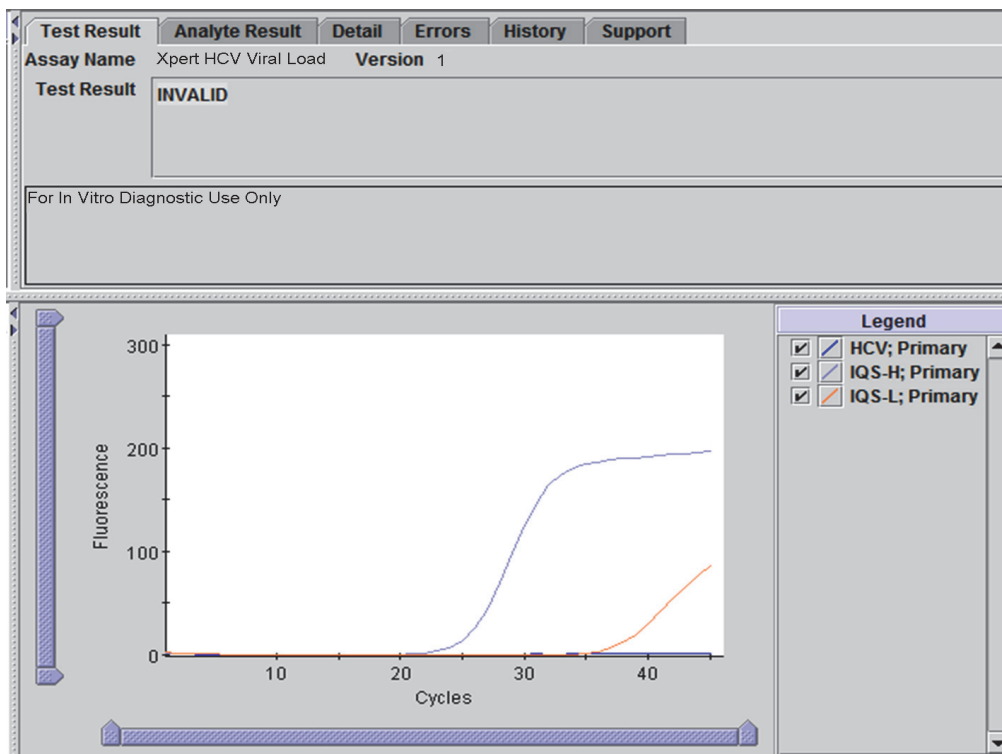


Figure 7. Invalid

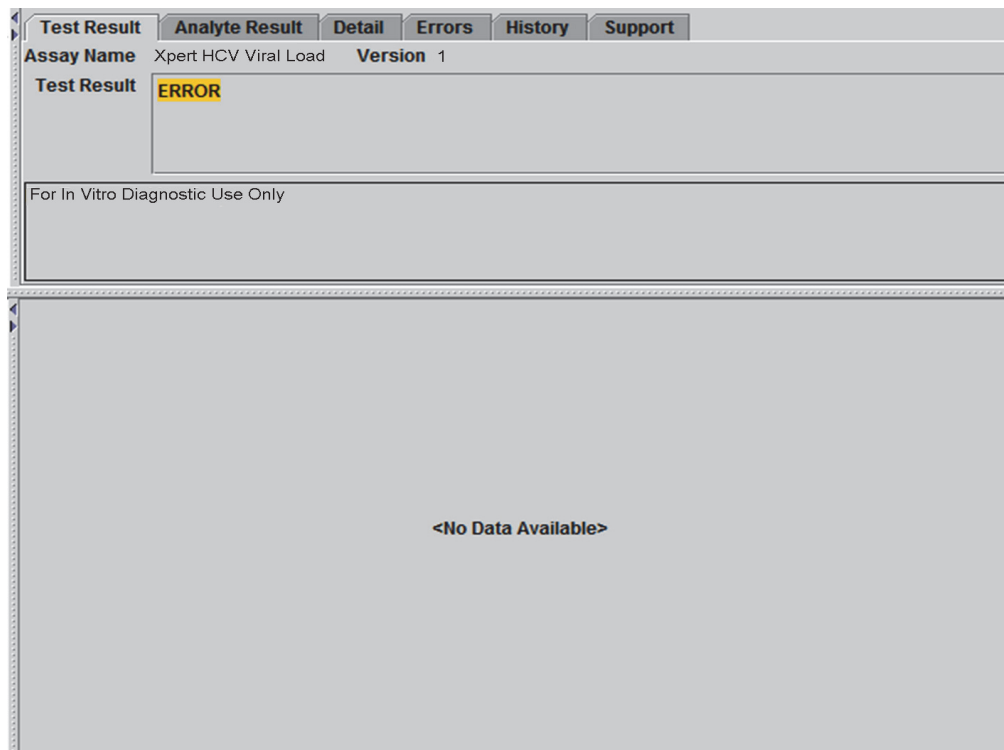


Figure 8. Error

## 16 Retests

### 16.1 Reasons to Repeat the Assay

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 IQS-H and/or IQS-L Cts are not within valid range.
  - 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 Specimen, Section 12.2, Preparing the Cartridge, and Section 12.3, Starting the Test.

## 17 Limitations

Good laboratory practices and changing gloves between handling specimens are recommended to avoid contamination of reagents.

## 18 Performance Characteristics

### 18.1 Limit of Detection

The limit of detection (LOD) of the HCV VL assay was determined by testing eight different dilutions prepared from a HCV genotype 1 reference standard in HCV negative EDTA plasma and serum. The HCV genotype 1 material used in the LOD study was the WHO 4th International standard, NIBSC code 06/102. The limit of detection was determined for three reagent lots and a total of 72 or 73 replicates per concentration level were tested. One additional low concentration level was included for both sample types after the first day of testing. The number of tested replicates for this level was thus smaller (49 in plasma and 53 in serum). The evaluation was performed according to CLSI guideline E17-A2. The HCV RNA concentration that can be detected with a positivity rate of greater than 95% was determined by Probit regression analysis and the results for the individual lots and specimens are shown in Table 2. The maximum observed LOD with Probit analysis for HCV genotype 1 in EDTA plasma is 4.0 IU/mL (95% CI 2.8 – 5.2). The maximum observed LOD with Probit analysis for HCV genotype 1 in serum is 6.1 IU/mL (95% CI 4.2 – 7.9).

**Table 2. HCV VL LOD Estimates with Probit Regression and 95% Upper and Lower Confidence Intervals for HCV Genotype 1 Specimens in Plasma and Serum per Kit Lot**

Specimen	Lot	LOD 95% (IU/mL)	95% CI (IU/mL)
WHO (Plasma)	1	3.3	2.4 - 4.2
	2	4.0	2.7 - 5.2
	3	4.0	2.8 - 5.2
WHO (Serum)	1	6.1	4.2 - 7.9
	2	2.6	1.9 - 3.3
	3	2.3	1.8 - 2.9

Hit rate analysis shows a positivity of > 95% at 6 IU/mL for the HCV genotype 1 material tested as shown in Table 3.

**Table 3. HCV VL LOD for HCV Genotype 1 in EDTA Plasma and Serum**

Specimen	Concentration (IU/mL)	No. Replicates	No. Positives	Positivity Rate (%)
WHO (Plasma)	0.5 <sup>a</sup>	49	24	49
	1	72	47	65
	2	72	61	85
	3	72	69	96
	4	72	67	93
	6	72	71	99
	8	73	73	100
	10	72	72	100
WHO (Serum)	0.5 <sup>a</sup>	53	21	40
	1	73	47	64
	2	73	64	88
	3	72	69	96
	4	73	71	97
	6	72	71	99
	8	72	70	97
	10	72	72	100

a. 0.5 IU/mL was added day 2 due to the high positivity rate observed at 1 IU/mL after day 1

In addition, dilutions of clinical specimens representing HCV genotype 1a, 2b, 3a, 4a, 5a and 6a in negative human EDTA plasma were analyzed with one reagent lot and 24 replicates per concentration level. The assignment of the nominal concentration of clinical specimens was determined by Abbott RealTime HCV™ assay. Hit rate analysis shows a positivity of >95% for all genotypes at 10 IU/mL as shown in Table 4.

**Table 4. HCV VL LOD Hit Rate Analysis for HCV Genotype 1 – 6 Specimens in EDTA Plasma**

Genotype	Lowest Concentration Level > 95% Hit Rate (IU/mL)	Hit Rate (%)
1a	10	100
2b	4	100
3a	6	100
4a	4	100
5a	2	96
6a	4	96

## 18.2 Limit of Quantitation

The total analytical error (TAE) was calculated using estimates determined through analysis of data from LOD study (WHO standard) and the Precision/Reproducibility study according to CLSI guideline E17-A2. The TAE for the dilutions that had an observed concentration at or near the assay limit of detection 10 IU/mL ( $1.0 \log_{10}$ ) are presented in Table 5. TAE was estimated by two different methods.

**Table 5. HCV VL TAE Analysis for Determination of LOQ**

Specimen (Study)	DL Lot	N	Concentration ( $\log_{10}$ IU/mL)		Bias	Total SD	TAE <sup>a</sup> Absolute Bias + 2xSD	TAE <sup>b</sup> 2xSQRT (2)xSD
			Expected	Observed				
Acrometrix (Precision)	DL1	72	1.40	1.31	0.09	0.15	0.38	0.41
	DL2	72	1.40	1.29	0.11	0.14	0.40	0.41
	DL3	72	1.40	1.24	0.16	0.12	0.41	0.35
Acrometrix (Precision)	DL1	72	1.00	0.92	0.08	0.22	0.52	0.62
	DL2	72	1.00	0.82	0.18	0.18	0.54	0.51
	DL3	72	1.00	0.75	0.25	0.19	0.63	0.54
WHO, Plasma (LOD)	DL1	24	1.00	0.91	0.09	0.21	0.51	0.59
	DL2	24	1.00	0.82	0.18	0.30	0.78	0.86
	DL3	24	1.00	0.86	0.14	0.17	0.48	0.48
WHO, Serum (LOD)	DL1	24	1.00	0.96	0.04	0.13	0.30	0.37
	DL2	24	1.00	0.88	0.12	0.23	0.58	0.66
	DL3	24	1.00	0.80	0.20	0.18	0.57	0.52

a. TAE calculated according to the Westgard model in CLSI EP17-A2 (Section 6.2)

b. TAE based upon the difference between two measurements approach

The results of the TAE analysis demonstrate that the HCV VL Assay can determine 10 IU/mL ( $1.0 \log_{10}$ ) with an acceptable trueness and precision.

**18.3 Precision/Reproducibility**

The precision/reproducibility of the HCV VL Assay was determined by analysis of parallel dilutions of HCV reference materials in HCV negative EDTA plasma. The nominal concentration of the reference material used was calibrated to the WHO 4th HCV International Standard (06/102). The study was a two site, blinded, comparative study using a seven-member panel of HCV reference material in HCV negative EDTA plasma with RNA concentrations that span the HCV VL Assay quantitation range. Two operators at each of the two study sites tested one panel of twenty-one samples once per day over six testing days per lot. One site used an Infinity-80 instrument and the other site used GeneXpert Dx instruments. Three lots of HCV VL Assay reagents were used for the study. Precision/reproducibility was evaluated in accordance with “Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline” CLSI document EP5-A2. The precision results for each reagent lot are shown in Table 6.

**Table 6. HCV VL Precision per Lot**

Expected HCV RNA Concentration log <sub>10</sub> IU/mL	Total Precision per Lot					
	Lot 1		Lot 2		Lot 3	
	SD	CV <sup>a</sup>	SD	CV <sup>a</sup>	SD	CV <sup>a</sup>
1.0	0.23	55.8%	0.18	44.2%	0.20	48.1%
1.4	0.15	35.1%	0.15	35.8%	0.13	29.6%
2.7	0.09	20.7%	0.09	20.6%	0.09	20.2%
4.2	0.07	16.4%	0.08	18.9%	0.07	15.3%
5.4	0.12	28.3%	0.09	19.9%	0.07	16.2%
6.9	0.13	31.8%	0.09	20.9%	0.07	17.0%
8.2	0.10	22.7%	0.10	23.7%	0.08	17.8%

a. “CV” is lognormal CV, as obtained using the formula:

$$CV(\text{of the lognormal dist}) = \sqrt{10^{\ln(10)^2 \sigma} - 1}$$



The reproducibility of the HCV VL Assay was evaluated by using nested ANOVA with terms for Site/Instrument, Lot, Day, Operator/Run and Within-Run. The standard deviation and the percentage of variability due to each component of the log<sub>10</sub> HCV transformed concentrations were calculated, see Table 7.

**Table 7. Standard Deviation and Contributable Percentage of Variability for Each Term and Total Precision**

HCV RNA Concentration log <sub>10</sub> IU/mL			Contribution to Total Variance SD (CV%)										Total Precision			
Expected	Actual	N	Site/Inst		Lot		Day		Operator/Run		Within-Run		Total			
			SD	(%) <sup>a</sup>	SD	(%) <sup>a</sup>	SD	(%) <sup>a</sup>	SD	(%) <sup>a</sup>	SD	(%) <sup>a</sup>	SD	Lower CI	Upper CI	CV <sup>b</sup>
1.0	0.83	216	0.03	1.8%	0.08	13.2%	0.04	3.5%	0.00	0.0%	0.19	81.6%	0.21	0.18	0.25	51.7%
1.4	1.28	216	0.00	0.0%	0.04	7.1%	0.00	0.0%	0.00	0.0%	0.14	92.9%	0.14	0.13	0.16	34.1%
2.7	2.66	216	0.00	0.0%	0.04	17.2%	0.00	0.0%	0.02	3.2%	0.08	79.5%	0.09	0.08	0.11	22.1%
4.2	4.18	215	0.00	0.0%	0.05	30.9%	0.01	2.6%	0.00	0.0%	0.07	66.5%	0.09	0.07	0.12	20.6%
5.4	5.44	216	0.00	0.0%	0.06	26.5%	0.00	0.0%	0.01	1.3%	0.09	72.2%	0.11	0.09	0.14	25.8%
6.9	6.86	216	0.00	0.0%	0.07	34.0%	0.02	3.4%	0.00	0.0%	0.10	62.5%	0.13	0.10	0.17	29.8%
8.2	8.11	216	0.00	0.0%	0.09	47.9%	0.00	0.0%	0.02	2.6%	0.09	49.5%	0.13	0.10	0.19	30.5%

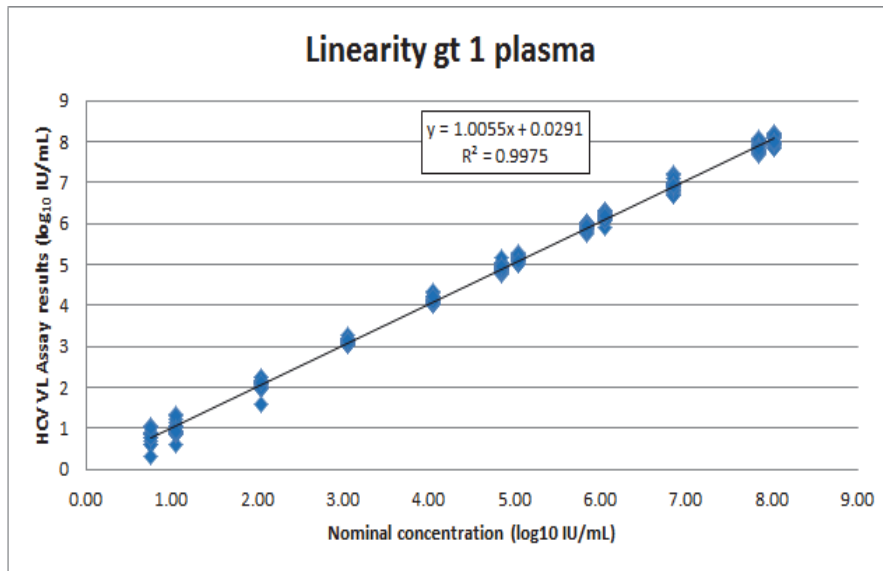
a. (%) is contribution of variance component to overall lognormal CV

b. "CV" is lognormal CV, as obtained using the formula:

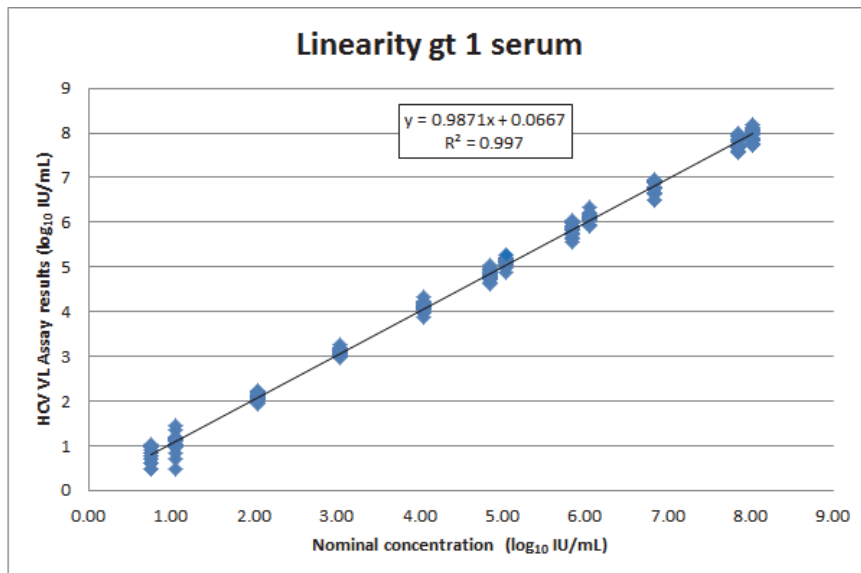
$$CV(\text{of the lognormal dist}) = \sqrt{10^{\ln(10) \cdot \sigma} - 1}$$

**18.4 Linear Range and Inclusivity**

The linear range of the HCV VL Assay was determined by analysis of a twelve member panel covering a range from ~5 (0.75 log<sub>10</sub>) to ~1 x 10<sup>8</sup> (8 log<sub>10</sub>) IU/mL. Panels were prepared by parallel dilutions of HCV reference material (armored RNA genotype 1 and clinical specimen genotype 1) in HCV negative EDTA plasma and serum. The nominal concentration of the reference material used was calibrated to the WHO 4th HCV International Standard (06/102). Each panel member was tested in replicates of four on each of three testing days using two kit lots. Totally, 24 replicates per panel member and sample type were tested. The linearity analysis was performed according to CLSI guideline EP06-A. The combined results for both lots are shown in Figure 9 and Figure 10. The HCV VL Assay is linear within a range 0.8–8.0 log<sub>10</sub> IU/mL with a R<sup>2</sup> value of >0.997.



**Figure 9. Linearity Genotype 1 in EDTA Plasma for the HCV VL Assay**



**Figure 10. Linearity Genotype 1 in Serum for the HCV VL Assay**

To confirm the linear range and evaluate the inclusivity of the HCV VL Assay, panels consisting of clinical specimens representing HCV genotype 2 – 6 and armored RNA when available (genotypes 2 and 3 only) were prepared in negative human EDTA plasma. 7 – 13 panel members per genotype covering as wide a range as possible, varying from ~ 0.9 – 6 log<sub>10</sub> IU/mL for genotype 5 to ~ 0.9 – 8.3 log<sub>10</sub> for genotype 3, were prepared and analyzed in replicates of four on each of three testing days using two kit lots. For each genotype, 24 replicates per panel member were tested. The nominal concentrations of the reference materials used were calibrated to the WHO 4th HCV International Standard (06/102). All genotypes responded linearly with R<sup>2</sup> values ranging from 0.994 – 0.998.

### 18.5 Analytical Specificity (Exclusivity)

The analytical specificity of the HCV VL Assay was evaluated by adding potentially cross-reacting organisms at 1 x 10<sup>5</sup> CFU/mL, copies/mL or TCID<sub>50</sub>/mL input concentration into HCV negative EDTA plasma and in plasma that contained ~25 IU/mL HCV reference material (clinical specimen genotype 1). Tested organisms are listed in Table 8.

**Table 8. Analytical Specificity Organisms**

Human Immunodeficiency virus 1
Human Immunodeficiency virus 2
Human T-cell lymphotropic virus I
Human T-cell lymphotropic virus II
<i>Candida albicans</i>
Cytomegalovirus
Epstein-Barr virus
Hepatitis A virus
Hepatitis B virus
Herpes simplex virus 1
Herpes simplex virus 2
Human herpes virus 6
Human herpes virus 8
Varicella Zoster virus
BK Human polyoma virus
Banji virus
Ilheus virus
West Nile virus
Zika virus
Human papilloma virus 16
Human papilloma virus 18
<i>Staphylococcus epidermidis</i>
<i>Staphylococcus aureus</i>

None of the tested organisms showed cross reactivity and all positive replicates resulted in concentrations of HCV RNA within ± 0.5 log from a HCV positive control when tested using the HCV VL Assay. In addition to the species listed in Table 8, Dengue virus and vaccinia virus were analysed *in silico* since material representing the viruses could not be obtained for testing. No practical significant sequence similarity was found between the analyzed viruses and the primers and probes of the Xpert HCV VL Assay.

**18.6 Potentially Interfering Substances**

The susceptibility of the HCV VL Assay to interference by elevated levels of endogenous substances, by drugs prescribed to HCV infected patients and by autoimmune disease markers was evaluated. HCV negative EDTA plasma and plasma that contained ~25 IU/mL HCV reference material (clinical specimen genotype 1) were tested.

Elevated levels of the endogenous substances listed in Table 9 were shown not to interfere with the quantification of the HCV VL Assay or impact the assay specificity.

**Table 9. Endogenous Substances and Concentration Tested**

Substance	Tested Concentration
Albumin	9 g/dL
Bilirubin	20 mg/dL
Hemoglobin	500 mg/dL
Human DNA	0.4 mg/dL
Triglycerides	3.0 mg/dL

The drug components as presented in Table 10 were shown not to interfere with the quantification of the HCV VL Assay or impact the assay specificity when tested at three times peak level concentration in five drug pools.

**Table 10. Drug Pools Tested**

Pool	Drugs
Control	N/A
1	Zidovudine, Saquinavir, Ritonavir, Interferon alfa-2b, Clarithromycin
2	Abacavir sulfate, Fosampervir Calcium, Peginterferon 2b, Ribavirin
3	Tenofovir disoproxil fumarate, Lamivudine (3TC), Indinavir sulfate, Ganciclovir, Valganciclovir HCl, Acyclovir
4	Stavudine (d4T), Efavirenz, Lopinavir, Enfuvirtide (T-20), Ciprofloxacin
5	Nevirapine, Nelfinavir mesylate, Azithromycin, Valacyclovir HCl

Testing of specimens from ten individuals per autoimmune disease marker shows no interference with the autoimmune disease markers systemic lupus erythematosus (SLE), anti-nuclear antibody (ANA), or rheumatoid factor (RF) using the HCV VL Assay.

### 18.7 Sample Collection Media Equivalence (EDTA, PPT-EDTA and Serum)

For each sample collection media (EDTA, PPT-EDTA and serum) specimens from 50 matched HCV positive individuals and 25 matched HCV negative specimens were collected and tested using one kit lot of the HCV VL Assay.

As shown in Figure 11 and Figure 12 equivalent performance of the HCV VL Assay was shown for EDTA plasma versus serum collection media and EDTA plasma versus PPT-EDTA plasma collection media. All HCV positive specimens collected in serum or PPT-EDTA plasma media produced concentrations of HCV RNA within  $\pm 0.5 \log_{10}$  IU/mL of the HCV positive specimen collected in EDTA plasma media when tested using the HCV VL Assay.

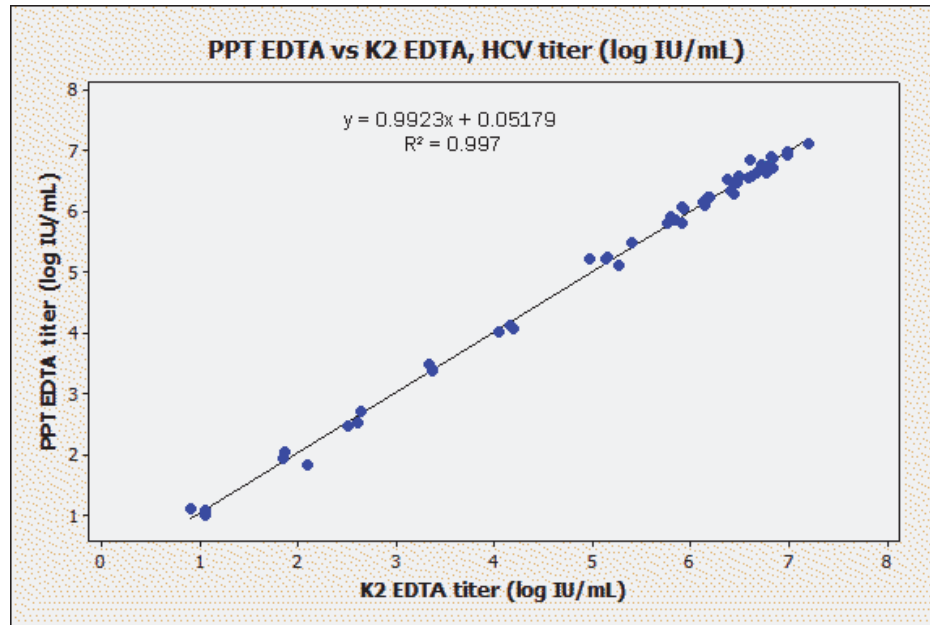


Figure 11. Scatterplot of Log IU/mL PPT-EDTA versus Log IU/mL EDTA

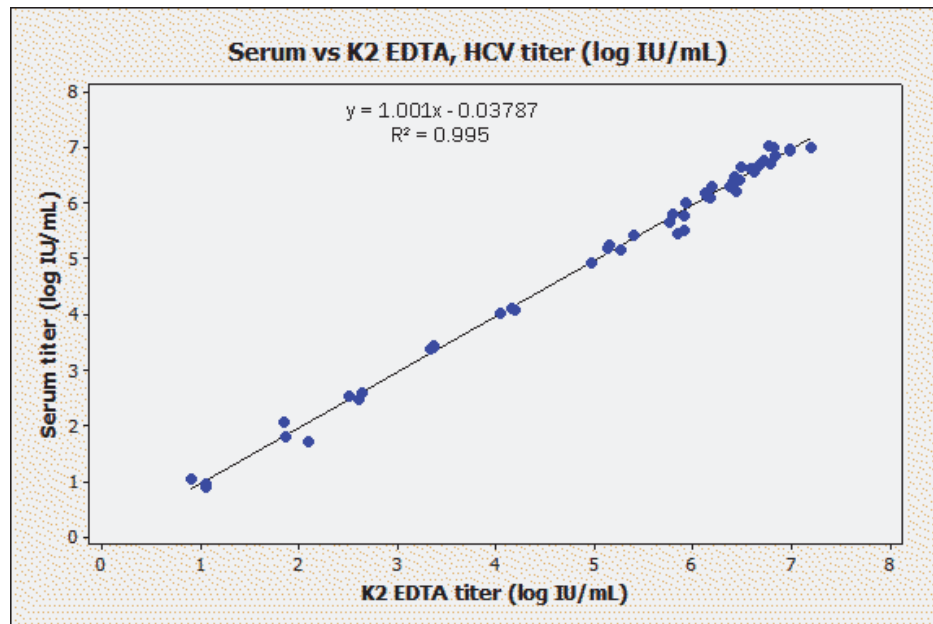


Figure 12. Scatterplot of Log IU/mL Serum versus Log IU/mL EDTA Plasma

## 19 Performance Characteristics – Clinical Performance

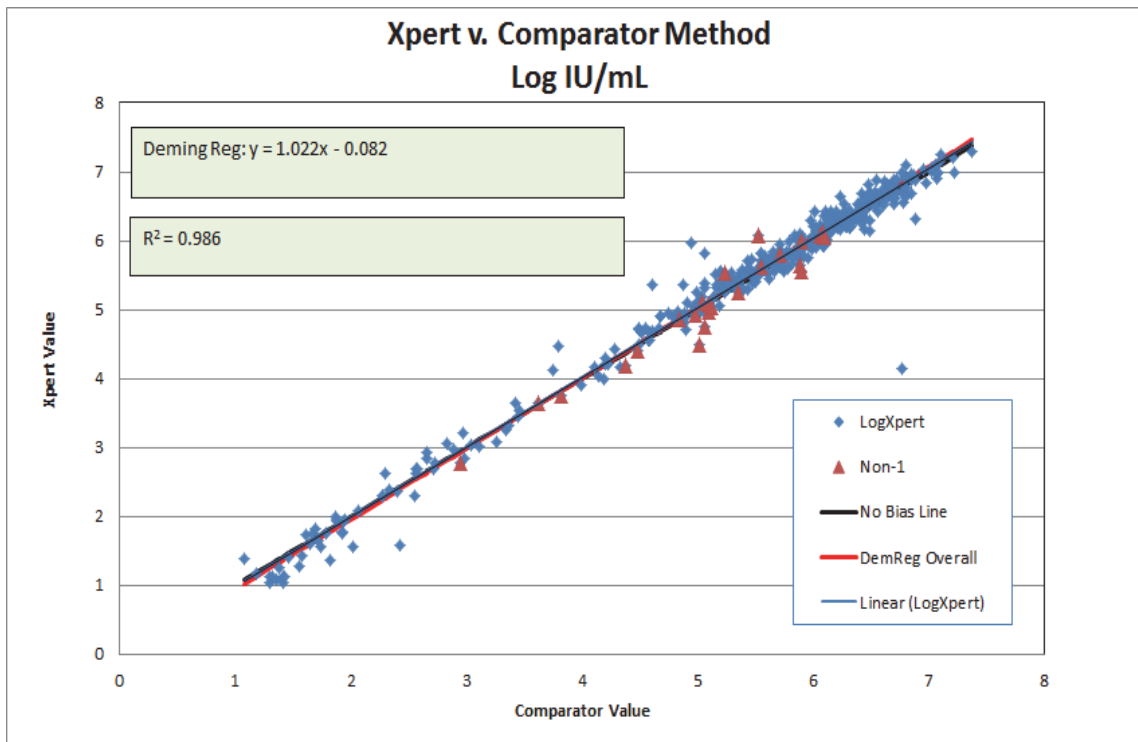
### Specificity

The specificity of the HCV VL assay was evaluated using 100 EDTA plasma specimens from HCV negative blood donors. None of the 100 specimens tested were detected by the HCV VL assay equating to 100% specificity (95% CI = 96.1-100).

### Method Correlation

A multi-site study was conducted to evaluate the performance of the HCV VL assay relative to a comparator method using fresh and frozen human plasma specimens collected from HCV infected individuals. Of the 607 eligible specimens, each from unique individuals, 408 (67.2%) were collected from male subjects. The average age was  $50.2 \pm 13.2$  years with an age range of 21 to 86 years.

Of the 607 specimens, 389 were within the quantitation range of both assays including 23 specimens that were HCV non-1 genotypes (2, 2a, 2b, 2c, 3, 3a, 4 & 6) and one mixed genotype (HCV 1 & 6). The Deming regression shows very good correlation between the HCV VL and the comparator method with a slope of 1.022 and intercept of 0.082. The  $R^2$  was 0.986.



\*HCV non-1 genotypes are represented as triangles. A single outlier was not included in the analysis.

**Figure 13. Xpert v. Comparator Method**

## 20 References

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11. REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on the classification labeling and packaging of substances and mixtures amending and repealing, List of Precautionary Statements, Directives 67/548/EEC and 1999/45/EC (amending Regulation (EC)).
12. Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z).

## 21 Cepheid Headquarters Locations

Corporate Headquarters	European Headquarters
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Telephone: +1 408.541.4191	Telephone: +33 563 825 300
Fax: +1 408.541.4192	Fax: +33 563 825 301
www.cepheid.com	www.cepheidinternational.com

## 22 Technical Assistance

Before contacting Cepheid Technical Support, collect the following information:














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

Region	Telephone	Email
US – Technical Support	+1 888.838.3222	TechSupport@cepheid.com
US – Technical Service	+ 1 888.838.3222	servicesupport@cepheid.com
France	+33 563 825 319	Support@cepheideurope.com
Germany	+49 69 710 480 480	Support@cepheideurope.com
Italy	+39 800 902 567	Support@cepheideurope.com
United Kingdom	+44 3303 332 533	Support@cepheideurope.com
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## 23 Table of Symbols

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



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