GeneXpert®
Powered By CEPHEID INNOVATION

Xpert® HPV v2

REF **GXHPV2-CE-10**

Instructions for Use

CE 2797 **IVD**

Cepheid®

In Vitro Diagnostic Medical Device

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See Revision History for a description of changes.

Xpert® HPV v2

For *in vitro* diagnostic use only.

1 Proprietary Name

Xpert® HPV v2

2 Common or Usual Name

Xpert HPV v2

3 Intended Purpose

3.1 Intended Use

The Xpert® HPV v2 test, performed on GeneXpert® systems, is an automated, qualitative, *in vitro* test for the detection of the E6/E7 region of the viral DNA genome from high risk Human Papillomavirus (HPV) in patient specimens. The test carries out multiplexed amplification of target DNA by real-time Polymerase Chain Reaction (PCR) of 14 high risk HPV types in a single analysis. Xpert HPV v2 specifically identifies types HPV 16 and HPV 18/45 in two distinct detection channels, and reports 11 other high risk types (31, 33, 35, 39, 51, 52, 56, 58, 59, 66 and 68) in a pooled result. Specimens are limited to cervical cells collected in PreservCyt® Solution (Hologic Corp.). Cervical specimens collected in PreservCyt Solution that have been pretreated with Glacial Acetic Acid (GAA) to lyse excess red blood cells for cytology review have also been validated for use with the Xpert HPV v2 test.

- The Xpert HPV v2 test can be used with a Pap specimen to assess the presence or absence of genotypes 16 and 18/45 and other high risk HPV genotypes in adult females who are at increased risk of developing cervical cancer or presence high-grade disease.
- The Xpert HPV v2 test can be used as a first-line primary screening test to identify adult females who are at increased risk of developing cervical cancer or the presence of high-grade disease.

This information, together with the physician's assessment of the patient's medical history, other risk factors, and professional guidelines, may be used to guide patient management.

3.2 Intended User/Environment

The Xpert HPV v2 test is intended to be performed by healthcare professionals trained on the use of the test. This test is for use in a laboratory environment.

4 Summary and Explanation

Persistent infection with high risk HPV is the main cause of cervical cancer and is a precursor to cervical intraepithelial neoplasia (CIN). HPV presence has been implicated in more than 99% of cervical cancers worldwide.HPV is estimated to be responsible for more than 90% of cervical cancers.[1] HPV is a small, non-enveloped, double-stranded DNA virus, with a genome of approximately 8,000 nucleotides. There are more than 150 different types of HPV, and approximately 40 types of HPV that can infect the human anogenital mucosa.[2] However, only a subset of approximately 14 of these types is considered high risk for the development of cervical cancer and its precursor lesions. Recent findings suggest that type-specific high

risk HPV-DNA-based screening tests and protocols should focus on HPV types 16, 18, and 45.[3] On a global basis, HPV types 16, 18, and 45 were found in 75% of all squamous carcinomas, and determined to be associated with approximately 80% of all invasive cervical cancers.[4,5]

Note In this publication "HPV" or "HR HPV" means "high risk HPV," unless noted otherwise.

5 Principle of the Procedure

The Xpert HPV v2 test is an automated test for qualitative detection and differentiation of HPV DNA. The test is performed on Cepheid GeneXpert ®Instrument Systems.

GeneXpert Instrument Systems automate and integrate sample processing, nucleic acid extraction and amplification, and detection of the target sequences in clinical samples by using real-time PCR. 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 contain the PCR reagents, and carry out the sample extraction and 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 System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

The Xpert HPV v2 test includes reagents for the detection of high-risk HPV. The Xpert HPV v2 test is designed for use with cervical specimens collected in PreservCyt with either a broom-like device or an endocervical brush/spatula combination. Cervical specimens pretreated with certain Glacial Acetic Acid (GAA) methods may also be used. Cervical specimens collected in PreservCyt Solution have been validated for use with the Xpert HPV v2 test. Follow the manufacturer's instructions for collecting cervical specimens.

A Sample Adequacy Control (SAC) and a Probe Check Control (PCC) are also included in the cartridge. SAC reagents detect the presence of a single copy human gene and monitor whether the specimen contains adequate numbers of human cells to carry out a qualitative assessment of HPV status. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The Xpert HPV v2 test contains primers and probes for the detection of specific genotypes or pooled results as follows: "SAC" for the Sample Adequacy Control, "HPV 16" for HPV 16, "HPV 18_45" for the HPV 18/45 pooled result, "P3" for the pooled result of any of HPV types 31, 33, 35 52, or 58, "P4" for the pooled result of either of HPV types 51 or 59, and "P5" for the pooled result of any of HPV types 39, 56, 66 or 68.

6 Reagents and Instruments

6.1 Materials Provided

The Xpert HPV v2 kit (GXHPV2-CE-10) contains sufficient reagents to process 10 quality control samples and/or specimens.

The kit contains the following:

Xpert HPV v2 cartridges		**10**
Component/Reagent	**Active Ingredient**	**Amount**
Beads (freeze dried)	Taq DNA Polymerase <50 U/bead	2 per cartridge
	Primers and probes < 0.001%	
	dNTPs < 0.05%	
	Primers and probes < 0.001%	
	Protein Stabilizer <0.5% (Bovine Origin)	
Reagent	Chelating Agent < 0.05%	2 mL per cartridge
	Tris Buffer < 0.5%	
	Detergent < 0.2%	
	Salt 1<0.3%	
	Ammonium sulfate < 0.3%	
	Salt 2 <0.1%	

The kit contains the following ingredients:

Kit Components	
Disposable 1 mL Transfer Pipettes	1 bag of 10 per kit
CD	1 per kit

- Assay Definition Files (ADF)
- Instructions to import ADF into GeneXpert software
- Instructions for Use (IFU)

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

Note The protein stabilizer (bovine origin) 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 postmortem testing. During processing, there was no mixing of the material with other animal materials.

6.2 Storage and Handling

- Store the Xpert HPV v2 test cartridges at 2–28 °C until the expiration date provided on the label.
- Do not open the cartridge lid until you are ready to perform the test.
- Do not use a cartridge that has leaked.
- Do not use a cartridge that previously has been frozen.
- Do not use a cartridge past the expiration date.

6.3 Materials Required but Not Provided

- Cervical specimen collected in PreservCyt with either a broom-like device or an endocervical brush/spatula combination
- GeneXpert Dx System or GeneXpert Infinity System (catalog number varies by configuration): GeneXpert instrument, computer with proprietary GeneXpert Software Version 4.3 or higher (GeneXpert Dx System) or Xpertise 6.1 or higher (GeneXpert Infinity System), barcode scanner, and appropriate GeneXpert system operator manual.
- Printer (If a printer is needed, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.)
- Bleach or sodium hypochlorite
- Ethanol or denatured ethanol

7 Warnings and Precautions

- For *in vitro* diagnostic use only.
- Pathogenic microorganisms, including hepatitis viruses and human immunodeficiency virus (HIV), may be present in clinical samples. Treat all biological samples, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological samples should be treated with standard precautions. Guidelines for sample handling are available from the U.S. Center for Disease Control and Prevention and the Clinical and Laboratory Standards Institute.[6,7]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- 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.
- Good laboratory practices and changing gloves between handling patient specimens are recommended to avoid contamination of specimens.
- Do not substitute Xpert HPV v2 reagents with other reagents.
- Do not open the Xpert HPV v2 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 cartridge may yield invalid results.
- Do not place the sample ID label on the cartridge lid or on the barcode label.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use Xpert HPV v2 cartridge is used to process one test. Do not reused processed cartridges.
- The single-use disposable pipette is used to transfer one specimen. Do not reuse spent disposable pipettes.
- Do not use cartridge which has been knocked over after adding sample.
- 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 concentration of 1:10 dilution of household chlorine bleach or sodium hypochlorite and then a 70% ethanol or 70% isopropanol solution. Whip work surfaces dry completely before proceeding.
- Appropriate safety measures should be taken in the event of a splash that may occur using bleach and facilities for adequate eye washing or skin rinsing are advised to care for such events.
- For Instrument System cleaning and disinfecting instructions, refer to the appropriate GeneXpert Dx System Operator Manual or GeneXpert Infinity System Operator Manual.

8 Chemical Hazards[9,10]

Ingredients are not considered hazardous under EU directives or regulations for classification and labeling of substances or mixtures or the Global Harmonization System for classification and labeling of substances or mixtures.

9 Specimen Collection, Transport, and Storage

- **Specimen Collection**

Cervical specimens collected in PreservCyt Solution have been validated for use with the Xpert HPV v2 test. Follow the manufacturer's instructions for collecting cervical specimens.

- **Specimen Transport**

  Cervical specimens collected in PreservCyt Solution can be transported at 2–30 ºC. Transportation of cervical specimens must comply with country, federal, state and local regulations for the transport of etiologic agents.

- **Specimen Storage**

  Cervical specimens collected in PreservCyt Solution may be stored at 2–30 °C for up to six months after the date of collection.

10 Procedure

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

10.1 Preparing the Specimen

Following mixing of the cervical sample, pipette minimum of 1mL sample directly into the test cartridge (see section 12.2).

- Mix the cervical sample by gently inverting the sample vial 8 to 10 times, or by vortexing briefly with a vortex mixer at half- speed continuously for 5 seconds.

10.2 Preparing the Cartridge

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

1. Wear protective disposable gloves.
2. Inspect the test cartridge for damage. If damaged, do not use it.
3. Label cartridge with sample identification.
4. Open the lid of the test cartridge.
5. Add the sample to the test cartridge.

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

- If using the transfer pipette included in the kit (Figure 1), open the sample vial lid, unwrap the transfer pipette, compress the transfer pipette bulb, insert the pipette into the vial, and release the bulb to fill the transfer pipette to the 1 mL line (Figure 1). Ensure the pipette is filled, with no air bubbles present. Expel the pipette’s contents into the sample chamber of the cartridge (Figure 2).

Important **Avoid adding excess mucus to the cartridge.**

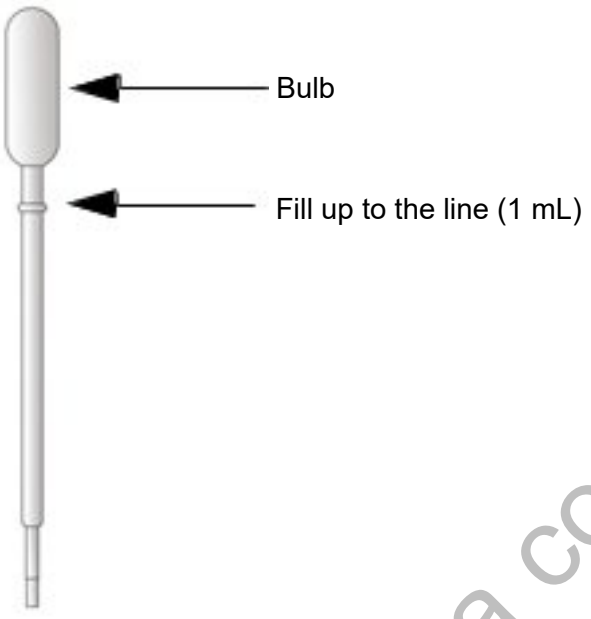

Figure 1. Transfer Pipette and Fill Mark

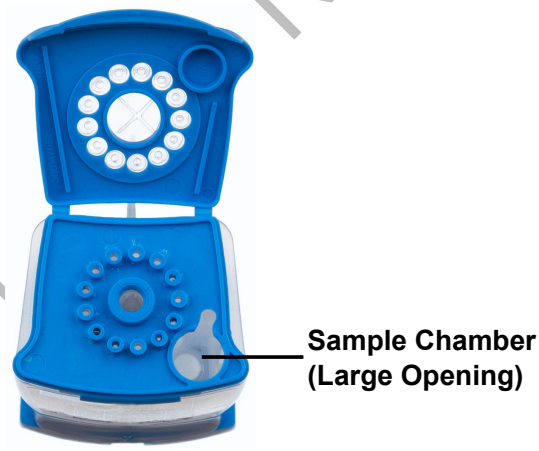

Figure 2. Xpert HPV v2 Cartridge (Top View)

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

10.3 Importing the Assay Definition Files

Important **Before you start the test, make sure the Xpert HPV v2 Assay Definition Files (ADF) are imported into the software.**

The Xpert HPV test can be configured to default to any one of the three ADFs at the discretion of the laboratory. Clinician requests for reflex genotyping of HPV 16 or HPV 18/45, can be ordered under the HPV genotype specific test, or where indicated, run as part of a full high risk and genotype test.

- High risk HPV only test: Select **Xpert HPV v2 HR** reports a positive or a negative overall result for the presence of any of the 14 high risk HPV types detected.
- HPV 16, 18/45 genotyping test: Select **Xpert HPV v2 16 18-45** reports a positive or a negative result for:

- HPV 16, and for
- HPV 18 or HPV 45 genotype.

  Specific results of all other HPV types are neither collected nor displayed.

- A combined high risk HPV and HPV genotype test: Select **Xpert HPV v2 HR 16 18-45** reports a positive or a negative result for HPV 16, for HPV 18/45, and for the presence of any of the remaining 11 other high risk types as "Other HR HPV." Only the test result for the test selected at this step will be collected once the test is started. Uncollected data are not recoverable.

11 Running the Test

- For the GeneXpert Dx System, see Section 11.1.
- For the GeneXpert Infinity System, see Section 11.2.

11.1 GeneXpert Dx System

11.1.1 Starting the Test

Before you start the test, make sure that:

Important

- The system is running the correct GeneXpert Dx software version shown in section - Materials Required but Not Provided.
- The correct assay definition file is imported into the software.

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual*.

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

1. Turn on the GeneXpert Dx System, then turn on the computer and log on. The GeneXpert software will launch automatically. If it does not, double-click the GeneXpert Dx software shortcut icon on the Windows® desktop.
2. Log on using your username and password.
3. In the **GeneXpert System** window, click **Create Test**.
   The **Create Test** window displays. The **Scan Patient ID barcode** dialog box displays.
4. Scan or type in the Patient ID. If typing the Patient ID, make sure the Patient ID is typed correctly.
   The Patient ID is associated with the test results and displays in the **View Results** window and all the reports. The **Scan Sample ID barcode** dialog box displays.
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 displays in the **View Results** window and all the reports. The **Scan Cartridge Barcode** dialog box displays.
6. Scan the barcode on the cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.

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

7. Click **Start Test**. In the dialog box that displays, type your password, if required.
8. Open the instrument module door with the blinking green light and load the cartridge.
9. Close the door. The test starts and the green light stops blinking.
   When the test is finished, the light turns off.
10. Wait until the system releases the door lock before opening the module door, then remove the cartridge.
11. Dispose of the used cartridges in the appropriate specimen waste containers according to your institution's standard practices.

11.1.2 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*.

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.

11.2 GeneXpert Infinity System

11.2.1 Starting the Test

Before you start the test, make sure that:

Important

- The system is running the correct Xpertise software version shown in section - Materials Required but Not Provided.
- The correct assay definition file is imported into the software.

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Infinity System Operator Manual*.

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

1. Power up the instrument. The Xpertise software will launch automatically. If it does not, double-click the Xpertise software shortcut icon on the Windows® desktop.
2. Log on to the computer, then log on to the GeneXpert Xpertise software using your user name and password.
3. In the **Xpertise Software Home** workspace, click **Orders** and in the **Orders** workspace, click **Order Test**. The **Order Test - Patient ID** workspace displays.
4. Scan or type in the Patient ID. If typing the Patient ID, make sure the Patient ID is typed correctly. The Patient ID is associated with the test results and displays in the **View Results** window and all the reports.
5. Enter any additional information required by your institution, and click the **CONTINUE** button. The **Order Test - Sample ID** workspace displays.
6. 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 displays in the **View Results** window and all the reports.
7. Click the **CONTINUE** button. The **Order Test - Assay** workspace displays.
8. Scan the barcode on the cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.

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

   After the cartridge is scanned, the **Order Test - Test Information** workspace displays.
9. Verify that the information is correct, and click **Submit**. In the dialog box that displays, type your password, if required.
10. Place the cartridge on the conveyor belt. The cartridge automatically loads, the test runs, and the used cartridge are placed into the waste container.

11.2.2 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 Infinity System Operator Manual*.

1. In the **Xpertise Software Home** workspace, click the **RESULTS** icon. The Results menu displays.
2. In the Results menu, select the **VIEW RESULTS** button. The **View Results** workspace displays showing the test results.
3. Click the **REPORT** button to view and/or generate a PDF report file.

12 Quality Control

Each test includes a Probe Check Control (PCC) and a Sample Adequacy Control (SAC).

- **Probe Check Control (PCC):** Before the PCR reaction starts, the GeneXpert instrument measures the fluorescence signal from the probes to monitor bead rehydration, reaction tube filling, probe integrity and dye stability. PCC passes if it meets the validated acceptance criteria.
- **Sample Adequacy Control (SAC):** The SAC reagents detect the presence of a single copy of human gene present in one copy per cell and monitor whether the sample contains human DNA.
- **External Controls:** External controls may be used in accordance with local, state, federal accrediting organizations, as applicable.

13 Interpretation of Results

The results are interpreted by the GeneXpert Instrument System from measured fluorescent signals and embedded calculation algorithms and will be shown on the Test Result tab of the View Results window. The Xpert HPV v2 test provides test results for HPV targets, according to the results and interpretations shown in Table 1.

Note Only the test results for the selected ADF will be collected once the test is started.

Table 1. Xpert HPV v2 Results and Interpretations

ADF	Result	Interpretation
Xpert HPV v2 HR	**HR HPV POS**	High risk HPV DNA is detected as positive. ● The targeted high risk HPV DNA has a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● SAC: Not applicable. The SAC is ignored because HPV target amplification can compete with this control. ● PCC: PASS; all probe check results pass.
	HR HPV NEG	High risk HPV DNA is below the level of detection. ● The targeted high risk HPV DNA has a Ct not within the valid range and/or a fluorescence endpoint below the threshold setting. ● SAC: PASS; PCR amplification of the SAC target gives a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● PCC: PASS; all probe check results pass.
Xpert HPV v2 16_18-45 and Xpert HPV v2 HR 16 18-45	**HPV 16 POS**	HPV 16 DNA is detected as positive. ● The targeted HPV 16 DNA has a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● SAC: Not applicable. The SAC is ignored because HPV target amplification can compete with this control. ● PCC: PASS; all probe check results pass.
	HPV 18_45 POS	HPV 18_45 DNA is detected as positive. ● The targeted HPV 18/45 DNA has a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● SAC: Not applicable. The SAC is ignored because HPV target amplification can compete with this control. ● PCC: PASS; all probe check results pass.

ADF	Result	Interpretation
Xpert HPV v2 16_18-45 and Xpert HPV v2 HR 16 18-45	**HPV 16 NEG**	HPV 16 DNA is below the level of detection. ● The targeted HPV 16 DNA has a Ct not within the valid range and/or a fluorescence endpoint below the threshold setting. ● SAC: PASS; PCR amplification of the SAC target gives a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● PCC: PASS; all probe check results pass.
	HPV 18_45 NEG	HPV 18-45 DNA is below the level of detection. ● The targeted HPV 18/45 DNA has a Ct not within the valid range and/or a fluorescence endpoint below the threshold setting. ● SAC: PASS; PCR amplification of the SAC target gives a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● PCC: PASS; all probe check results pass.
Xpert HPV v2 HR 16 18-45	**OTHER HR HPV POS**	Other high-risk HPV DNA is detected as positive. ● The targeted other high risk HPV DNA has a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● SAC: Not applicable. The SAC is ignored because other high risk HPV target amplification can compete with this control. ● PCC: PASS; all probe check results pass.
	OTHER HR HPV NEG	Other high risk HPV DNA is below the level of detection. ● The targeted other high risk HPV DNA has a Ct not within the valid range and/or a fluorescence endpoint below the threshold setting. ● SAC: PASS; PCR amplification of the SAC target gives a Ct within the valid range and a fluorescence endpoint above the threshold setting. ● PCC: PASS; all probe check results pass.
Applies to all ADFs	**INVALID**	Presence or absence of HPV target DNA cannot be determined. Repeat the test according to the instructions in Retest Procedure. ● SAC: FAIL; SAC Ct is not within the valid range and/or a fluorescence endpoint below the threshold setting. ● PCC: PASS; all probe check results pass.
	ERROR	Presence or absence of HPV target DNA cannot be determined. Repeat the test according to the instructions in Retest Procedure. ● SAC: NO RESULT ● PCC: FAIL*; all or one of the probe check results fail. * If the probe check passed, the error is caused by the maximum pressure limit exceeding the acceptable range or by a system component failure.
	NO RESULT	Presence or absence of HPV target DNA cannot be determined. Repeat the test according to the instructions in Retest Procedure. 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. ● HPV: NO RESULT ● SAC: NO RESULT ● PCC: NA (not applicable)

14 Retests

14.1 Reasons to Repeat the Test

If any of the following test results occur, repeat the test according to instructions in Retest Procedure.

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

14.2 Retest Procedure

- If the result of a test is **INVALID**, **ERROR**, or **NO RESULT**, use a new cartridge to retest the affected sample. (Do not re-use the cartridge)
- Remove new cartridge from the kit.
- Obtain the leftover sample.
- Go to Section 10, Procedure.
- If the leftover sample volume is insufficient, or the retest continues to return an **INVALID**, **ERROR**, or **NO RESULT**, collect a new sample and repeat the test with a new cartridge.

15 Limitations

- Because the detection of HPV is dependent on the DNA present in the sample, reliable results are dependent on proper sample collection, handling, and storage.
- The Xpert HPV v2 test has only been validated with cervical specimens collected in PreservCyt Solution using either a broom-like device or an endocervical brush/spatula combination.
- Erroneous test results might occur from improper specimen collection, technical error, sample mix-up, or because the HPV DNA copy number is below the limit of detection of the test.
- The Xpert HPV v2 test has been validated using the procedures provided in this package insert only. Modification to these procedures may alter the performance of the test.
- Assay interference may be observed in the presence of: whole blood (≥ 0.25% v/v), peripheral blood mononuclear cells (PBMC) (≥ 1 x 10^6 cells/mL), *Candida albicans* (≥ 1 x 10^8 cells/mL), Vagisil anti-itch cream (≥ 0.25% w/v) or Vagi Gard moisturizing gel (≥ 0.5% w/v).
- The presence of thick vaginal creams (> 0.25% w/v) in the sample may result in pressure aborts.
- The effects of other potential variables such as vaginal discharge, use of tampons, douching, and specimen collection variables have not been determined.
- The Xpert HPV v2 test provides qualitative results. No correlation can be drawn between the magnitude of the Ct value and the number of cells in an infected sample.
- Xpert HPV v2 test performance has not been evaluated in patients less than 18 years of age.
- Xpert HPV v2 test performance has not been evaluated in women with a history of hysterectomy.
- The Xpert HPV v2 test has not been validated for use with vaginal swab specimens collected by a physician or a patient.
- The Xpert HPV v2 test has not been evaluated with patients who are currently being treated with antimicrobial agents for infections such as chlamydia or gonorrhea.
- As with many diagnostic tests, results from the Xpert HPV v2 test should be interpreted in conjunction with other laboratory and clinical data available to the physician.
- The performance of the Xpert HPV v2 test has not been evaluated for HPV-vaccinated individuals.
- The Xpert HPV v2 test has not been evaluated in cases of suspected sexual abuse.
- Prevalence of HPV infection in a population may affect performance.
- Samples containing less than 1 mL of PreservCyt Solution are considered inadequate for the Xpert HPV v2 test.

- Xpert HPV v2 test performance has not been evaluated in cervical specimens preprocessed for cytology review using processors other than the ThinPrep 2000 Processor.
- A negative Xpert HPV v2 test result does not exclude the possibility of cytologic abnormalities or of future or underlying CIN2, CIN3, or cancer.
- The Xpert HPV v2 test detects E6/E7 viral DNA of the high risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. This test does not detect E6/E7 DNA of HPV low risk types (e.g., 6, 11, 42, 43, 44) since there is no clinical utility for assessing the presence of low risk types of HPV in the context of cervical cancer screening.
- Detection of high risk HPV DNA is dependent on the number of copies present in the specimen and may be affected by specimen collection methods, patient factors, stage of infection, and the presence of interfering substances.
- Use of this product must be limited to personnel trained in the use of the Xpert HPV v2 test.
- False Positive or False Negative results may occur with this test.
- Mutations or polymorphisms in primer or probe binding regions may affect detection of targeted HPV types resulting in a false negative result.

16 Clinical Performance

Clinical performance characteristics of the Xpert HPV v2 test were assessed in a two-stage, multicenter [seven US sites], prospective study that enrolled women of all ages referred for colposcopy evaluation. Referral was based on one or more prior abnormal Pap test results, an abnormal Pap test result in combination with a positive high risk HPV test result, or other clinical suspicion of cervical cancer. Two ThinPrep specimens (Specimen A and Specimen B) were collected from each subject at the time of colposcopy to support cytology review and comparator testing with the Xpert HPV v2 test and two FDA-approved, high risk HPV tests. Analyses with these comparator methods were conducted per the respective US-IVD Package Inserts. Specimen A was processed for cytology review followed by analysis with the Xpert HPV v2 test. Specimen B was reserved for HPV analysis with the comparator HPV tests and the Xpert HPV v2 test. Both specimens were collected using an endocervical brush/spatula combination per the ThinPrep Package Insert. A minimum of two cervical punch biopsies were collected from each subject as well as an ECC for unsatisfactory colposcopy evaluations in which there was poor visualization of the squamocolumnar junction. Pathology review of the biopsy and endocervical curettage (ECC) specimens was first conducted locally for standard of care/patient management and then retrospectively, in blinded fashion, by a panel of three expert review pathologists to determine a consensus final cervical disease status. Stage I of recruitment included 144 subjects (age range: 20–70 years) with 31 cases ≥ CIN2. Data from Stage I was used to estimate a set of clinical cutoffs for the test relative to ≥ CIN2 and ≥ CIN3 disease end points using a Receiver Operating Characteristic (ROC) approach. Stage II of recruitment included 564 subjects (age range: 18–75 years) with 111 cases ≥ CIN2. Data from Stage II was used to refine the clinical cutoffs relative to ≥ CIN2 and ≥ CIN3 disease end points using an ROC approach. Retrospectively, a homogeneity analysis was conducted to confirm the poolability of results from Stage I and Stage II; across multiple population and specimen parameters, the results are poolable.

Clinical sensitivity and specificity of the Xpert HPV v2 test, comparator method 1, and comparator method 2 in the Stage II data set relative to a ≥ CIN2 disease status, are summarized in Table 2.

Table 2. Clinical Performance Relative to ≥ CIN2 Disease Status[a]

	Xpert HPV v2 Test (Specimen A)[b]	Xpert HPV v2 Test (Specimen B)[c]	Comparator Method 1[d]	Comparator Method 2[e]
Sensitivity	(99/109) 90.8% (83.8 – 95.5%)	(100/110) 90.9% (83.9 – 95.6%)	(103/111) 92.8% (86.3 – 96.8%)	(96/111) 86.5% (78.7 – 92.2%)
Specificity	(182/429) 42.4% (37.7 – 47.3%)	(194/446) 43.5% (38.8 – 48.2%)	(178/453) 39.3% (34.8 – 44.0%)	(212/451) 47.0% (42.3 – 51.7%)
Positive Predictive Value	(99/346) 28.6% (23.8 – 33.7%)	(100/352) 28.4% (23.8 – 33.4%)	(103/378) 27.2% (22.8 – 32.0%)	(96/335) 28.7% (23.9 – 33.8%)

	Xpert HPV v2 Test (Specimen A)[b]	Xpert HPV v2 Test (Specimen B)[c]	Comparator Method 1[d]	Comparator Method 2[e]
Negative Predictive Value	(182/192) 94.8% (90.6 – 97.5%)	(194/204) 95.1% (91.2 – 97.6%)	(178/186) 95.7% (91.7 – 98.1%)	(212/227) 93.4% (89.3 – 96.3%)

[a] Point estimates are as indicated. Confidence intervals are Fisher-Exact 95% CI.

[b] n = 538. Nine specimens QNS for Xpert testing; 17 specimens indeterminate upon initial and retest.

[c] n = 556. Eight specimens indeterminate upon initial and retest.

[d] n = 564.

[e] n = 562. Two specimens indeterminate upon initial and retest.

Clinical sensitivity and specificity of the Xpert HPV v2 test, comparator method 1, and comparator method 2 in the Stage II data set relative to a ≥ CIN3 disease status are summarized in Table 3.

Table 3. Clinical Performance Relative to ≥ CIN3 Disease Status[a]

	Xpert HPV v2 Test (Specimen A)[b]	Xpert HPV v2 Test (Specimen B)[c]	Comparator Method 1[d]	Comparator Method 2[e]
Sensitivity	(68/72) 94.4% (86.4 – 98.5%)	(69/73) 94.5% (86.6 – 98.5%)	(71/74) 95.9% (88.6 – 99.2%)	(64/74) 86.5% (76.5 – 93.3%)
Specificity	(187/465) 40.2% (35.7 – 44.8%)	(199/482) 41.3% (39.6 – 45.8%)	(182/489) 37.2% (32.9 – 41.7%)	(216/487) 44.4% (39.9 – 48.9%)
Positive Predictive Value	(68/346) 19.7% (15.6 – 24.2%)	(69/352) 19.6% (15.6 – 24.1%)	(71/378) 18.8% (15.0 – 23.1%)	(64/335) 19.1% (15.0 – 23.7%)
Negative Predictive Value	(187/191) 97.9% (94.7 – 99.4%)	(199/203) 98.0% (95.0 – 99.5%)	(182/185) 98.4% (95.3 – 99.7%)	(216/226) 95.6% (92.0 – 97.9%)

[a] Point estimates are as indicated. Confidence intervals are Fisher-Exact 95% CI.

[b] n = 537. Nine specimens QNS for Xpert testing; 17 specimens indeterminate upon initial and retest; consensus on CIN2 vs. CIN3status not reached for one specimen.

[c] n = 555. Eight specimens indeterminate upon initial and retest; consensus on CIN2 vs. CIN3 status not reached for one specimen.

[d] n = 563. Consensus on CIN2 vs. CIN3 status not reached for one specimen.

[e] n = 561. Two specimens indeterminate upon initial and retest; consensus on CIN2 vs. CIN3 status not reached for one specimen.

An assessment of analytical agreement in the Stage II data set demonstrated overall agreement between the Xpert HPV v2 test and itself (Specimen A vs. Specimen B; n = 533 paired comparisons) of 94.6% (95% CI 92.3 – 96.3; Kappa statistic 0.88). Overall agreement between the Xpert HPV v2 test (Specimen B) and comparator method 1 (n = 556 paired comparisons) was 92.4% (95% CI 89.9 – 94.5; Kappa statistic 0.83). Overall agreement between the Xpert HPV v2 test (Specimen B) and comparator method 2 (n = 554 paired comparisons) was 87.4% (95% CI 84.3 – 90.0; Kappa statistic 0.73).

Clinical performance of the Xpert HPV v2 test for Pap test specimen A and B, sorted by subject age group, was determined for both disease status ≥ CIN2 and ≥ CIN3. The clinical performance relative to ≥ CIN2 disease is presented in Table 4 and the clinical performance relative to ≥ CIN3 disease is presented in Table 5.

Table 4. Xpert HPV v2 Test Performance vs. ≥ CIN2 Disease, by Age Group

	Pap A		Pap B	
Age Group	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Sensitivity (95% CI)**	**Specificity (95% CI)**
20–29	95.7% (85.5 – 99.5)	25.8% (19.1 – 33.4)	95.7% (85.5 – 99.5)	32.1% (24.9 – 39.9)
30–39	91.7% (77.5 – 98.2)	46.4% (38.3 – 54.6)	94.6% (81.8 – 99.3)	44.3% (36.4 – 52.4)
40–49	88.9% (65.3 – 98.6)	44.8% (32.6 – 57.4)	88.9% (65.3 – 98.6)	45.8% (34.0 – 58.0)
50–59	71.4% (29.0 – 96.3)	62.8% (46.7 – 77.0)	71.4% (29.0 – 96.3)	64.4% (48.8 – 78.1)
≥ 60	100% (2.5 – 100)	33.3% (9.9 – 65.1)	100% (2.5 – 100)	30.8% (9.1 – 61.4)

Table 5. Xpert HPV v2 Test Performance vs. ≥ CIN3 Disease, by Age Group

	Pap A		Pap B	
Age Group	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Sensitivity (95% CI)**	**Specificity (95% CI)**
20–29	96.7% (82.8 – 99.9)	23.8% (17.7 – 30.9)	100% (88.4 – 100)	30.1% (23.4 – 37.5)
30–39	90.9% (70.8 – 98.9)	43.1% (35.5 – 51.0)	91.3% (72.0 – 98.9)	40.7% (33.3 – 48.4)
40–49	92.9% (66.1 – 99.8)	43.7% (31.9 – 56.0)	92.9% (66.1 – 99.8)	44.7% (33.3 – 56.6)
50–59	100% (39.8 – 100)	62.2% (46.5 – 76.2)	100% (39.8 – 100)	63.8% (48.5 – 77.3)
≥ 60	100% (2.5 – 100)	33.3% (9.9 – 65.1)	100% (2.5 – 100)	30.8% (9.1 – 61.4)

A second clinical study was conducted to assess the performance of the Xpert HPV v2 test in populations that more closely resemble the intended use populations served by organized cervical cancer screening programs. This study was a multicenter, method comparison study relying on residual specimens collected in PreservCyt obtained from women 20–60 years of age participating in organized cervical cancer screening programs in the UK. With rare exception, all of the specimens collected in this study were collected with a broom-like device per the ThinPrep Package Insert. The same two comparator methods were included in this study, with comparator method 1 as the primary comparator method and comparator method 2 as the secondary comparator method. Sample sizes for the study were calculated for two age groups (women ages 20–29 and women ages 30–60) that would support agreement assessment (with 95% CI) and calculation of a Kappa statistic (with 95% CI) relative to each comparator method.

In this study, residual specimens with cytology evaluation results were divided into three aliquots for assessment with the Xpert HPV v2 test and comparator methods 1 and 2. The sequence of aliquot removal for analysis with the Xpert HPV v2 and comparator method 1 was randomized such that ~50% of the first aliquots were used for Xpert HPV v2 analysis

and 50% of the first aliquots were used for comparator method 1. The third aliquot was always reserved for analysis with comparator method 2. Regardless of aliquot sequence, the source specimen vial was mixed before the removal of each aliquot to ensure specimen homogeneity. Analysis with the comparator methods was completed per the respective CE-IVD Package Inserts, which procedurally, were identical to the US-IVD Package Inserts; analysis of results utilizes the cutoff parameters from the US-IVD Package Inserts.

An analysis of study data demonstrated substantial agreement between the Xpert HPV v2 test and comparator method 1. This agreement is independent of subject age category (ages 20–29 and ages 30–60) and cytology status [normal (NILM, Negative for Intraepithelial Lesion or Malignancy) and worse than normal (worse than NILM)]. A summary of agreement between the Xpert HPV v2 test and comparator method 1 is shown in Table 6.

Table 6. Agreement between Xpert HPV v2 Test and Comparator Method 1

Agreement Comparison	n	Positive Percent Agreement	Negative Percent Agreement	Overall Percent Agreement	Kappa Statistic
Overall[a]	3,418	90.43% (87.89 – 92.56%)	97.1% (96.4 – 97.7%)	95.8% (95.1 – 96.5%)	0.87 (0.85 – 0.89)
Ages 20–29	833	92.97% (89.4 – 95.42%)	94.9% (92.6 – 96.7%)	94.1% (92.2 – 95%)	0.88 (0.84 – 0.91)
Ages 30–60	2,585	87.8% (83.7 – 91.2%)	97.6% (96.9 – 98.2%)	96.4% (95.6 – 97.1%)	0.84 (0.81 – 0.87)
Cytology Normal	2,975	85.1% (81.0 – 88.6%)	97.14% (96.6 – 98.0%)	95.8% (95.1 – 96.6%)	0.81 (0.78 – 0.854)
Cytology > Normal	443	96.7% (93.9 – 98.4%)	91% (84.9 – 95.0%)	94.8% (92.3 – 96.7%)	0.88 (0.83 – 0.93)

[a] Point estimates are as indicated. Confidence intervals are Fisher-Exact 95% CI.

An analysis of study data demonstrates good agreement between the Xpert HPV v2 test and comparator method 2. This agreement is independent of subject age category (ages 20–29 and ages 30–60) and cytology status [normal (NILM) and worse than normal (worse than NILM)]. A summary of agreement between the Xpert HPV v2 test and comparator method 2 is shown in Table 7.

Table 7. Agreement between Xpert HPV v2 Test and Comparator Method 2

Agreement Comparison	n	Positive Percent Agreement	Negative Percent Agreement	Overall Percent Agreement	Kappa statistic
Overall[a]	3,418	84.5% (81.8 – 87.34%)	96.5% (95.7 – 97.2%)	94.1% (93.0 – 94.7%)	0.82 (0.79 – 0.84)
Ages 20–29	833	94.2% (91.1 – 96.5%)	93.3% (90.7 – 95.3%)	93.6% (91.8 – 95.2%)	0.87 (0.83 – 0.90)
Ages 30–60	2,858	76% (71.2 – 80.3%)	97.2% (96.5 – 97.9%)	94.2% (93.3 – 95.1%)	0.75 (0.71 – 0.79)
Cytology normal	2,975	77.9% (73.3 – 82.2%)	96.6% (95.9 – 97.3%)	94.3% (93.4 – 95.1%)	0.74 (0.70 – 0.78)
Cytology > normal	443	92.5% (89.0 – 95.1%)	93.6% (87.8 – 97.2%)	92.8% (90.0 – 95.0%)	0.83 (0.77 – 0.89)

[a] Point estimates are as indicated. Confidence intervals are Fisher-Exact 95% CI.

As an additional measure of analytical agreement, the HPV positivity rate by cytology status was assessed in this study. In similar-sized samples of specimens assessed by each method, the HPV positivity rates reported by the three HPV methods are similar and in general agreement with HPV positivity rates reported in other low disease prevalence populations (e.g., the ALTS Study). A summary of the HPV positivity rates as measured by each method according to cytology status is shown in Table 8.

Table 8. HPV Positivity by Method and Cytology Status

	Xpert HPV v2 Assay			Comparator Method 1			Comparator Method 2		
Category (UK/US)	**Total**	**Pos**	**% Pos (95% CI)**	**Total**	**Pos**	**% Pos (95% CI)**	**Total**	**Pos**	**% Pos (95% CI)**
Normal / NILM	2,975	374	12.6 (11.4-13.8)	2,975	362	12.2 (11.0-13.4)	2,975	367	12.3 (11.2-13.6)
Borderline / ASC-US	215	113	52.6 (45.7-59.4)	215	108	50.2 (43.4-57.1)	215	120	55.8 (48.9-62.6)
Low-grade dyskaryosis (mild) / LSIL[a]	149	116	77.9 (70.3-84.2)	149	120	80.5 (73.3-86.6)	149	126	84.6 (77.7-90.0)
High-grade dyskaryosis	28	28	100.0 (87.7-100)	28	27	96.4 (81.7-99.9)	28	28	100.0 (87.7-100)
High-grade dyskaryosis (severe) / HSIL[b]	35	35	100.0 (90.0-100)	35	34	97.1 (85.1-99.9)	35	35	100.0 (90.0-100)
Other	16	10	62.5 (35.4-84.8)	16	10	62.5 (35.4-84.8)	16	9	56.3 (29.9-80.2)
Total	3,418	676	19.9 (18.5-21.2)	3,418	661	19.3 (18.0-20.7)	3,418	685	20.0 (18.7-21.4)

[a] Low grade squamous intraepithelial lesion.

[b] High grade squamous intraepithelial lesion.

A subset [249/3538 (7.8%)] of the specimens enrolled in this study was pretreated with Glacial Acetic Acid (GAA) prior to HPV assessment with the Xpert HPV v2 test and the comparator methods. One site utilized a modified version of a commercial methodology [71/1169 (6.1%)]; CytoLyt, Hologic, Crawley, UK, EU), while the other two sites used laboratory

developed procedures based on the Espostis method [153/1170 (13.1%) and 25/1198 (2.1%), respectively].[11–13] The Xpert HPV v2 test demonstrates good agreement to the comparator methods independent of GAA pretreatment status. See Table 9 and Table 10.

Table 9. Agreement between Xpert HPV v2 Test and Comparator Method 1 in GAA Pretreated Specimens[a]

Agreement Comparison	n	Positive Percent Agreement	Negative Percent Agreement	Overall Percent Agreement	Kappa Statistic
GAA Pretreated	245	94.3% (86.0-98.4)	96.6% (92.7 – 98.7%)	95.9% (92.6 – 98.0%)	0.90 (0.84 – 0.96)
Untreated	3,173	89.8% (87.1 – 92.2%)	97.2% (96.5 – 97.8%)	95.8% (95.1 – 96.5%)	0.86 (0.84 – 0.89)

[a] Point estimates are as indicated. Confidence intervals are Fisher-Exact 95% CI.

Table 10. Agreement between Xpert HPV v2 Test and Comparator Method 2 in GAA Pretreated Specimens[a]

Agreement Comparison	n	Positive Percent Agreement	Negative Percent Agreement	Overall Percent Agreement	Kappa Statistic
GAA Pretreated	245	87.3% (72.9 – 94.0%)	94.3% (89.7 – 97.2%)	92.2% (88.2 – 95.3%)	0.81 (0.73 – 0.89)
Untreated	3,173	84.4% (81.2 – 87.0%)	96.6% (95.9 – 97.3%)	94.3% (93.4 – 95.0%)	0.82 (0.79 – 0.84)

[a] Point estimates are as indicated. Confidence intervals are Fisher-Exact 95% CI.

17 Analytical Performance

17.1 Limit of Detection

The analytical sensitivity or limit of detection (LoD) of the Xpert HPV v2 test was assessed using:

1. HPV positive cell lines: HPV 16 (SiHa), HPV 18 (HeLa S3), HPV 45 (MS751) and HPV 68 (ME180) in PreservCyt solution containing an HPV negative cell line (C33A) background, and
2. DNA plasmids of the 14 targeted high risk HPV types in a background of human female genomic DNA.

HPV Positive Cell Lines

The LoD for HPV 16, HPV 18, HPV 45, and HPV 68 was estimated by running replicates of 20 at a minimum of six concentrations for each of the cell lines using one kit lot of the Xpert HPV v2 test. LoDs were estimated by probit analysis. The claimed LoDs were verified by analyzing at least 20 replicates diluted to the estimated LoD concentrations using three kit lots of the Xpert HPV v2 test. The claimed LoD is defined as the concentration at which 95% of at least 20 replicates per reagent lot are positive (Table 11).

HPV DNA Plasmids

The LoD for 14 high risk HPV DNA plasmids was confirmed with a minimum of 60 replicates across two operators and three lots. Tests were run on different days. The level (in copies per PCR reaction) at which the overall true positive rate is statistically greater than 95% pooled across three reagent lots was determined for each of the HPV DNA plasmids (Table 12).

Table 11. Limit of Detection: HPV Positive Cell Lines

HPV Type	LoD Est. by Probit (Cells/mL)	95% CI	99.9% CI	Conf. Level (Cells/mL)	Reagent Lot	Pos of 20 Rep.	Ct Avg. (Target)	Ct Stdev (Target)	Overall Ct Avg. (Target)	Overall Ct Stdev (Target)	% Pos	Overall % Pos
16	71	55 – 87	52 – 127	122	Lot 1	19	35.6	1.0	35.3	1.2	95	95.0
					Lot 2	19	35.0	1.4			95	
					Lot 3	19	35.4	1.2			95	
18	46	35 – 56	33 – 90	53	Lot 1	20	36.0	1.2	35.6	1.1	100	96.7
					Lot 2	19	35.3	0.9			95	
					Lot 3	19	35.6	1.1			95	
45	180	150 – 211	142 – 266	173	Lot 1	19	37.0	1.2	37.1	1.1	95	96.7
					Lot 2	20	37.0	1.2			100	
					Lot 3	19	37.4	0.9			95	
68	267	231 – 304	221 – 366	366	Lot 1	20	35.9	0.6	36.0	0.6	100	96.7
					Lot 2	19	35.9	0.7			95	
					Lot 3	20	36.2	0.5			100	

Table 12. Limit of Detection: HPV DNA Plasmids

Target	Copy Level Tested	Sample Count	FN	% Pos	Lower 1-sided 95% CI	Ct Grand Avg.	Ct Stdev
HPV 35	15	60	0	100	95.1%	33.9	0.426
HPV 39	20	60	0	100	95.1%	36.5	0.352
HPV 45	10	100	0	100	97.0%	35.6	0.533
HPV 51	10	100	0	100	97.0%	35.1	0.587
HPV 52	15	60	0	100	95.1%	34.7	0.543
HPV 56	15	101	0	100	97.1%	36.6	0.525
HPV 58	20	60	0	100	95.1%	33.7	0.412
HPV 59	10	100	0	100	97.0%	35.1	0.618
HPV 66	30	60	0	100	95.1%	36.6	0.33
HPV 68	15	100	0	100	97.0%	36.9	0.445
HPV 16	10	100	0	100	97.0%	35.1	0.559
HPV 18	10	141	1	99.3	96.7%	35.9	0.585
HPV 31	10	100	0	100	97.0%	34.2	0.529
HPV 33	10	100	0	100	97.0%	35.0	0.642

18 Assay Precision and Reproducibility

Precision and reproducibility of the Xpert HPV v2 test was assessed in a 12-day, multicenter study in which two operators at each of three sites blindly tested a 16-member precision panel, twice daily. This panel was composed of both contrived samples (cultured cells containing different types of HPV in a background of non-HPV-containing cultured cells) and pooled clinical specimens in PreservCyt. Each site utilized a different configuration of GeneXpert System (one site used only GX IVs, one site used a GX XVI, and one site used an Infinity 80). Three lots of the Xpert HPV v2 test were used for each four-

day period of study testing. At the end of the study, each member of the precision panel was assessed 144 times. Data are summarized by assay channel, represented as 16 for the HPV 16 channel, 18/45 for the HPV 18 and HPV 45 channel, 31 for the HPV 31 and other types channel, 51 for the HPV 51 and HPV 59 channel, and 39 for the HPV 39 and other types channel. See Table 13 and Table 14.

Table 13. Xpert HPV v2 Precision and Reproducibility: Panel Description and Positive Agreement [a], [b]

Specimen (Target and Relative Concentration)	Assay Channel	Site 1		Site 2		Site 3		Total Agreement
		Op1	Op2	Op1	Op2	Op1	Op2	
Contrived Specimen (HPV 16 High Negative)	16	83.3% (20/24)	91.7% (22/24)	87.5% (21/24)	82.6% (19/23)	100% (23/23)	83.3% (20/24)	88.0% (125/142)
	18/45	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (142/142)
	31	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (142/142)
	51	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (142/142)
	39	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (142/142)
Contrived Specimen (HPV 16 Low Positive)	16	87.5% (21/24)	95.7% (22/23)	95.8% (23/24)	100% (23/23)	95.8% (23/24)	95.8% (23/24)	95.1% (135/142)
	18/45	100% (24/24)	100% (23/23)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (142/142)
	31	100% (24/24)	100% (23/23)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (142/142)
	51	100% (24/24)	100% (23/23)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (142/142)
	39	100% (24/24)	100% (23/23)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (142/142)
Contrived Specimen (HPV 16 Moderate Positive)	16	100% (24/24)	100% (24/24)	100% (24/24)	100% (21/21)	95.8% (23/24)	100% (24/24)	99.3% (140/141)
	18/45	100% (24/24)	100% (24/24)	100% (24/24)	100% (21/21)	100% (24/24)	100% (24/24)	100% (141/141)
	31	100% (24/24)	100% (24/24)	100% (24/24)	100% (21/21)	100% (24/24)	100% (24/24)	100% (141/141)
	51	100% (24/24)	100% (24/24)	100% (24/24)	100% (21/21)	100% (24/24)	100% (24/24)	100% (141/141)

Specimen (Target and Relative Concentration)	Assay Channel	Site 1		Site 2		Site 3		Total Agreement
		Op1	Op2	Op1	Op2	Op1	Op2	
	39	100% (24/24)	100% (24/24)	100% (24/24)	100% (21/21)	100% (24/24)	100% (24/24)	100% (141/141)
Contrived Specimen (HPV 18 High Negtive)	16	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (142/142)
	18/45	83.3% (20/24)	86.4% (19/22)	79.2% (19/24)	87.5% (21/24)	95.8% (23/24)	91.7% (22/24)	87.3% (124/142)
	31	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (142/142)
	51	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (142/142)
	39	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (142/142)
Contrived Specimen (HPV 18 Low Positive)	16	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (144/144)
	18/45	100% (24/24)	100% (24/24)	91.7% (22/24)	95.8% (23/24)	91.7% (22/24)	100% (24/24)	96.5% (139/144)
	31	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (144/144)
	51	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (144/144)
	39	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (144/144)
Contrived Specimen (HPV 18 Moderate Positive)	16	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (24/24)	100% (23/23)	100% (141/141)
	18/45	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (24/24)	100% (23/23)	100% (141/141)
	31	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (24/24)	100% (23/23)	100% (141/141)
	51	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (24/24)	100% (23/23)	100% (141/141)
	39	100% (24/24)	100% (23/23)	100% (23/23)	100% (24/24)	100% (24/24)	100% (23/23)	100% (141/141)

Specimen (Target and Relative Concentration)	Assay Channel	Site 1		Site 2		Site 3		Total Agreement
		Op1	Op2	Op1	Op2	Op1	Op2	
Contrived Specimen (HPV 68 High Negative)	16	100% (22/22)	100% (22/22)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (139/139)
	18/45	100% (22/22)	100% (22/22)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (139/139)
	31	100% (22/22)	100% (22/22)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (139/139)
	51	100% (22/22)	100% (22/22)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (139/139)
	39	90.9% (20/22)	95.5% (21/22)	100% (24/24)	91.3% (21/23)	91.7 (22/24)	91.7 (22/24)	93.5% (130/139)
Contrived Specimen (HPV 68 Low Positive)	16	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (23/23)	100% (24/24)	100% (141/141)
	18/45	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (23/23)	100% (24/24)	100% (141/141)
	31	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (23/23)	100% (24/24)	100% (141/141)
	51	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (23/23)	100% (24/24)	100% (141/141)
	39	95.8% (23/24)	95.8% (23/24)	100% (23/23)	87.0% (20/23)	100% (23/23)	100% (24/24)	96.5% (136/141)
Contrived Specimen (HPV 68 Moderate Positive)	16	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (142/142)
	18/45	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (142/142)
	31	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (142/142)
	51	100% (22/22)	100% (24/24)	100% (24/24)	95.8% (23/24)	100% (24/24)	100% (24/24)	100% (142/142)
	39	100% (22/22)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	95.8% (23/24)	99.3% (141/142)

Specimen (Target and Relative Concentration)	Assay Channel	Site 1		Site 2		Site 3		Total Agreement
		Op1	Op2	Op1	Op2	Op1	Op2	
Contrived Specimen (HPV 16/45/68 Low Positive)	16	100% (24/24)	100% (23/23)	95.8% (23/24)	95.8% (23/24)	95.7% (22/23)	100% (24/24)	97.9% (139/142)
	18/45	87.5% (21/24)	95.7% (22/23)	79.2% (19/24)	87.5% (21/24)	95.7% (22/23)	95.8% (23/24)	90.1% (128/142)
	31	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (23/23)	100% (24/24)	100% (142/142)
	51	100% (24/24)	100% (23/23)	100% (24/24)	95.8% (23/24)	100% (23/23)	100% (24/24)	99.3% (141/142)
	39	91.7% (22/24)	95.7% (22/23)	91.7% (22/24)	91.7% (22/24)	95.7% (22/23)	95.8% (23/24)	93.7% (133/142)
Contrived Specimen (Negative)	16	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (23/23)	100% (23/23)	100% (140/140)
	18/45	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (23/23)	100% (23/23)	100% (140/140)
	31	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (23/23)	100% (23/23)	100% (140/140)
	51	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (23/23)	100% (23/23)	100% (140/140)
	39	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (23/23)	100% (23/23)	100% (140/140)
Pooled Clinical Specimen (HPV 16, HPV 31)	16	50.0% (12/24)	20.8% (5/24)	33.3% (8/24)	18.2% (4/22)	8.3% (2/24)	20.8% (5/24)	25.4% (36/142)
	18/45	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)
	31	20.8% (5/24)	41.7% (10/24)	37.5% (9/24)	50.0% (11/22)	20.8% (5/24)	33.3% (8/24)	33.8% (48/142)
	51	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)
	39	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)

Specimen (Target and Relative Concentration)	Assay Channel	Site 1		Site 2		Site 3		Total Agreement
		Op1	Op2	Op1	Op2	Op1	Op2	
Pooled Clinical Specimen (HPV 18, HPV 39)	16	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (144/144)
	18/45	16.7% (4/24)	20.8% (5/24)	41.7% (10/24)	25.0% (6/24)	12.5% (3/24)	20.8% (5/24)	22.9% (33/144)
	31	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (144/144)
	51	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (144/144)
	39	4.2% (1/24)	4.2% (1/24)	0% (0/24)	8.3% (2/24)	0% (0/24)	0% (0/24)	2.8% (4/144)
Pooled Clinical Specimen (HPV 42, HPV 51, HPV 59)	16	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	95.8% (23/24)	100% (24/24)	99.3% (142/143)
	18/45	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (143/143)
	31	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (143/143)
	51	25.0% (6/24)	33.3% (8/24)	29.2% (7/24)	34.8% (8/23)	12.5% (3/24)	16.7% (4/24)	25.2% (36/143)
	39	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (24/24)	100% (24/24)	100% (143/143)
Pooled Clinical Specimen (HPV 52)	16	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (142/142)
	18/45	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (142/142)
	31	20.8% (5/24)	41.7% (10/24)	33.3% (8/24)	41.7% (10/24)	8.7% (2/23)	30.4% (7/23)	29.6% (42/142)
	51	95.8% (23/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (142/142)
	39	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (23/23)	100% (23/23)	100% (142/142)
Pooled Clinical Specimen (Negative)	16	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)

Specimen (Target and Relative Concentration)	Assay Channel	Site 1		Site 2		Site 3		Total Agreement
		Op1	Op2	Op1	Op2	Op1	Op2	
	18/45	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)
	31	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)
	51	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)
	39	100% (24/24)	100% (24/24)	100% (24/24)	100% (22/22)	100% (24/24)	100% (24/24)	100% (142/142)

[a] Agreement for negative and high negative specimens is shown as % negative; low and moderate positive specimen agreement shown as % positive.

[b] Study included 34 total indeterminates: HPV 16 high neg(2); HPV 16 low pos(2); HPV 18 mod pos(3); HPV 18 high neg(3); HPV 18 mod pos(3); HPV 68 high neg(5); HPV 68 low pos(3); HPV 68 mod pos(2); HPV 16, 45, 68(2); CP-negative(4); HPV 16, 31(2); HPV 42, 51, 59 (1); HPV 52(2); PC-negative(2).

Table 14. Xpert HPV v2 Reproducibility: Ct Variability for Panel Members[a]

Specimen (Target and Relative Concentration)	Assay Channel (Specific Analyte)	n[b]	Mean Ct	Between Sites		Between Operators		Between Lots		Between Day		Within Assay		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Contrived Specimen (HPV 16 High Negative)	16 (16)	12	38.4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Contrived Specimen (HPV 16 Low Positive)	16 (16)	135	35.4	0	0	0.605	1.7	0.425	1.2	0	0	1.003	2.8	1.246	3.5
Contrived Specimen (HPV 16 Moderate Positive)	16 (16)	140	34.0	0	0	0.288	0.8	0.211	0.6	0	0	0.972	2.9	1.036	3.0
Contrived Specimen (HPV 18 High Negative)	18/45 (18)	22	39.2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Contrived Specimen (HPV 18 Low Positive)	18/45 (18)	139	35.9	0	0	0.408	1.1	0.414	1.2	0	0	1.149	3.2	1.287	3.6
Contrived Specimen (HPV 18 Moderate Positive)	18/45 (18)	140	34.1	0	0	0	0	0.430	1.3	0.170	0.5	1.049	3.1	1.146	3.4
Contrived Specimen (HPV 68 High Negative)	39 (68)	116	39.5	0	0	0.811	2.1	0.296	0.7	0	0	1.025	2.6	1.340	3.4
Contrived Specimen (HPV 68 Low Positive)	39 (68)	141	36.2	0.055	0.2	0.362	1.0	0.099	0.3	0.265	0.7	0.703	1.9	0.843	2.3
Contrived Specimen (HPV 68 Moderate Positive)	39 (68)	142	34.7	0	0	0.060	0.2	0.196	0.6	0	0	0.789	2.3	0.815	2.3
Contrived Specimen (HPV 16/45/68 Low Positive)	16 (16)	140	35.4	0.042	0.1	0.497	1.4	0.124	0.4	0	0	1.171	3.3	1.278	3.6
	18/45 (45)	133	37.2	0	0	0	0	0.454	1.2	0	0	1.586	4.3	1.649	4.4
	39 (68)	141	36.4	0.056	0.2	0	0	0	0	0.280	0.8	0.876	2.4	0.922	2.5
Contrived Specimen (Negative)	Negative (HMBS)	140	28.9	0.126	0.4	0.323	1.1	0.115	0.4	0	0	0.714	2.5	0.802	2.8
Pooled Clinical Specimen (HPV 16, HPV 31)	16 (16)	41	37.5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	31 (31)	97	38.2	0	0	0	0	0.356	0.9	0.453	1.2	1.411	3.7	1.524	4.0
Pooled Clinical Specimen (HPV 18, HPV 39)	18 (16)	47	39.7	0.643	1.6	0	0	0	0	1.148	2.9	1.388	3.5	1.913	4.8
	39 (39)	61	39.8	0	0	0.741	1.9	0	0	0	0	1.197	3.0	1.408	3.5
Pooled Clinical Specimen (HPV 42, HPV 51, HPV 59)	ND (42)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	51 (51)	92	38.9	0.452	1.2	0	0	0	0	0.088	0.2	1.348	3.5	1.424	3.7
	59 (59)	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Pooled Clinical Specimen (HPV 52)	31 (52)	82	38.2	0.307	0.8	0	0	0	0	0	0	2.738	7.2	2.756	7.2
Pooled Clinical Specimen (Negative)	Negative (HMBS)	142	33.3	0.132	0.4	0	0	0.559	1.7	0	0	0.876	2.6	1.047	3.1

[a] NA indicates insufficient continuous data to perform an ANOVA analysis.

[b] Results with non-zero Ct values out of 144.

19 Analytical Specificity

A panel of 47 organisms, including bacteria, fungi, and viruses commonly found in the female urogenital tract, as well as 12 closely related Human Papilloma virus types, were tested with the Xpert HPV v2 test. All organisms were spiked into HPV negative cells (C33A) in PreservCyt solution and into HPV negative cells spiked with HPV 16 positive cells (SiHa) at three times the limit of detection. The organisms and test concentrations are listed in Table 15. The analytical specificity was 100% and none of the organisms interfered with detection of HPV 16.

Table 15. Analytical Specificity Panel

Organism	Test Concentration	Organism	Test Concentration
Bacteriodes fragilis	1 x 10^8CFU/mL	*Streptococcus agalactiae*	1 x 10^8CFU/mL
Bifidobacterium adolescentis	1 x 10^8CFU/mL	*Streptococcus pyogenes*	3 x 10^6CFU/mL
Bifidobacterium breve	1 x 10^8CFU/mL	*Trichomonas vaginalis*	1 x 10^6CFU/mL
Candida albicans	4 x 10^6cells/mL	Adenovirus	1 x 10^6TCID50/mL
Candida glabrata	1 x 10^8cells/mL	Cytomegalovirus (CMV)	1 x 10^7copies/mL
Chlamydia trachomatis	1 x 10^8EB[a]/mL	Epstein Barr virus (EBV)	1 x 10^7copies/mL
Clostridium perfringens	3 x 10^7CFU/mL	Hepatitis B virus (HBV)	3.6 x 10^6IU/mL
Corynebacterium xerosis	1 x 10^7cells/mL	Hepatitis C virus (HCV)	7.62 x 10^2IU/mL
Enterobacter cloacae	1 x 10^8CFU/mL	Human immunodeficiency virus 1 (HIV-1)	1 x 10^6copies/mL
Enterococcus faecalis	1 x 10^8CFU/mL	Herpes simplex virus 1 (HSV-1)	1 x 10^7copies/mL
Escherichia coli	1 x 10^8CFU/mL	Herpes simplex virus 2 (HSV-2)	1 x 10^7copies/mL
Fusobacterium nucleatum	8.7 x 10^7CFU/mL	Human papillomavirus (HPV) 6	1.25 x 10^7copies/mL
Klebsiella pneumoniae	1 x 10^8CFU/mL	HPV 11	1.25 x 10^7copies/mL
Lactobacillus acidophilus	1 x 10^7cells/mL	HPV 26	1.25 x 10^7copies/mL
Lactobacillus crispatus	1 x 10^7cells/mL	HPV 30	1.25 x 10^7copies/mL
Lactobacillus delbrueckii	1 x 10^7cells/mL	HPV 34	1.25 x 10^7copies/mL
Lactobacillus jensenii	3 x 10^7CFU/mL	HPV 53	1.25 x 10^7copies/mL
Neisseria gonorrhoeae	1 x 10^8CFU/mL	HPV 67	1.25 x 10^7copies/mL
Peptostreptococcus anaerobius	1 x 10^8CFU/mL	HPV 69	1.25 x 10^7copies/mL
Proteus mirabilis	1 x 10^8CFU/mL	HPV 70	1.25 x 10^7copies/mL
Proteus vulgaris	1 x 10^8CFU/mL	HPV 73	1.25 x 10^7copies/mL
Pseudomonas aeruginosa	1 x 10^8CFU/mL	HPV 82	1.25 x 10^7copies/mL
Staphylococcus aureus	1 x 10^8CFU/mL	HPV 85	1.25 x 10^7copies/mL
Staphylococcus epidermidis	3 x 10^6CFU/mL		

[a] Elementary Bodies.

20 Potentially Interfering Substances

Potentially interfering endogenous and exogenous substances that may be present in cervical specimens were evaluated relative to the performance of the Xpert HPV v2 test. Substances were individually diluted into HPV negative cells spiked with HPV 16 positive cells (SiHa) at three times the limit of detection. The substances and test concentrations are listed in Table 16. Interference was observed with whole blood (0.25% v/v) in the test sample, but not with any of the other endogenous substances at the given test concentrations. Interference was not observed with any of the exogenous substances at the given test concentrations, except for Vagisil anti-itch cream (0.25% w/v) and Vagi Gard Moisturizing Gel (0.5% w/v). Thick creams may result in pressure aborts at concentrations above 0.25% w/v in the test sample.

Table 16. Potentially Interfering Substances

Substance	Concentration
Whole blood	0.25% v/v
Mucus	0.15% v/v
Leukocytes (PBMC)	1 x 10^5cells/mL
Vagisil Anti-Itch Cream	0.25% w/v
Clotrimazole Vaginal Cream	0.25% w/v
Preparation H Hemorrhoidal Cream	0.25% w/v
Miconazole 3	0.25% w/v
Monistat 1	0.25% w/v
Zovirax Cold Sore Cream	0.25% w/v
Vagisil Moisturizer	10% w/v
Vagi-Gard Moisturizing Gel	0.5% w/v
KY Jelly Personal Lubricant	10% w/v
Yeast Gard Douche	10% v/v
Delfen Vaginal Contraceptive Foam	10% w/v
VH Essentials Povidone-Iodine Medicated Douche	10% v/v
Norforms Feminine Deodorant Suppositories	10% w/v

21 Carry-over Contamination

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination into negative samples run following very high positive samples in the same GeneXpert module. The study consisted of a negative sample processed within the same GeneXpert module immediately following a very high HPV 16 positive sample (high enough to exceed 95% of the results obtained from specimens of diseased patients in the intended use population). This testing scheme was repeated 20 times on two GeneXpert modules for a total of 42 runs resulting in 20 positive and 22 negative samples. All 20 positive samples were correctly reported as HPV 16 positive and all 22 negative samples were correctly reported as HPV negative.

22 Summary of Safety and Performance

Summary of Safety and Performance for the Xpert HPV v2 test is available on EUDAMED (https://ec.europa.eu/tools/eudamed).

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Authorized Representative

CH REP

Cepheid Switzerland GmbH
Zürcherstrasse 66
Postfach 124, Thalwil
CH-8800
Switzerland

Importer

Cepheid Switzerland GmbH
Zürcherstrasse 66
Postfach 124, Thalwil
CH-8800
Switzerland

25 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

Report serious incidents associated with the test to Cepheid and the competent authority of the member state in which the serious incident occurred.

United States Technical Support

Telephone: + 1 888 838 3222
Email: techsupport@cepheid.com

France Technical Support

Telephone: + 33 563 825 319
Email: support@cepheideurope.com

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

26 Table of Symbols

Symbol	Meaning
	Catalogue number
	*In vitro* diagnostic medical device
	Do not reuse
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of Manufacture
	Contains sufficient for *n* tests
	Control
	Use-by date
	CE marking – European Conformity
	Temperature limit
	Biological risks
	Authorized Representative in Switzerland
	Importer

CE 2797 IVD

27 Revision History

Initial release of 302-6157 Rev. A

Section	Description of Change
27	Release of BSI approved 302-6157 Rev. 2 into production Rev. A.