GeneXpert®
Powered By CEPHEID INNOVATION

Xpert® TV

REF **GXTV-CE-10**

Cepheid® ***In Vitro*** **Diagnostic Medical Device** CE IVD

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Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089
USA
Pnone: + 1 408 541 4191
Fax: + 1 408 541 4192

EC REP

Cepheid Europe SAS
Vira Solelh
81470 Maurens-Scopont
France
Pnone: + 33 563 825 300
Fax: + 33 563 825 301

Xpert® TV

For *in vitro* diagnostic use only.

1 Proprietary Name

Xpert® TV

2 Common or Usual Name

Xpert TV Assay

3 Intended Use

The Cepheid Xpert TV Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test for the detection of *Trichomonas vaginalis* genomic DNA. The test utilizes automated real-time polymerase chain reaction (PCR) to detect *Trichomonas vaginalis* genomic DNA. The Xpert TV Assay uses female and male urine specimens, endocervical swab specimens, or patient-collected vaginal swab specimens (collected in a clinical setting). The Xpert TV Assay is intended to aid in the diagnosis of trichomoniasis in symptomatic or asymptomatic individuals.

4 Summary and Explanation

The protozoan *Trichomonas vaginalis* is responsible for trichomoniasis, which is a common sexually transmitted infection that can infect both men and women. There are 7.4 million cases of trichomoniasis annually in the United States. Trichomoniasis infections can be symptomatic or asymptomatic.[1]

In women, trichomoniasis is one of a range of conditions that comprise vaginal discharge. Symptoms in females can include itching, burning, redness, or soreness of the genitals, unusual odor, discomfort with urination, or a thin clear, white, yellow, or green discharge.[2] In men, trichomoniasis may cause non-gonococcal urethritis (NGU). Symptoms in males can include itching or burning inside the penis, burning after ejaculation or urination, or penile discharge.[2,3]

5 Principle of the Procedure

The Xpert TV Assay is an automated *in vitro* diagnostic test for qualitative detection of *Trichomonas vaginalis* (TV). The assay is performed on Cepheid GeneXpert Instrument System.

The GeneXpert Instrument System automates and integrates sample preparation, nucleic acid extraction and amplification, and detection of the target sequence in simple or complex samples using reverse transcriptase polymerase chain reaction (RT-PCR) and/or real-time PCR assays. 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 real-time PCR reagents and host the reverse transcriptase PCR and real-time 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 TV Assay includes reagents for the detection of *Trichomonas vaginalis*. The Xpert TV Assay is designed for use with the following specimens collected from symptomatic and asymptomatic individuals: first-catch female and male urine, endocervical and vaginal swab specimens. The urine transport reagent and swab transport reagent are designed to preserve patient specimens during transport to the laboratory for analysis with Xpert TV Assay and are included in the following specimen collection kits: Xpert Urine Specimen Collection Kit, the Xpert Swab Specimen Collection Kit, and the Xpert Vaginal/ Endocervical Specimen Collection Kit.

A Sample Processing Control (SPC), a Sample Adequacy Control (SAC), and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate processing of the target sample and to monitor the presence of inhibitors in the PCR reaction. The SAC reagents detect the presence of a single copy human gene and monitor whether the specimen contains human cells. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

An Early Assay Termination function provides positive results if target DNA reaches a predetermined threshold before the full 45 PCR cycles have been completed. When TV levels are high enough to generate very early Cts, neither the SAC nor SPC amplification curves will be seen and their results will not be reported.

6 Reagents and Instruments

6.1 Material Provided

The Xpert TV Assay kit (GXTV-CE-10) contains sufficient reagents to process 10 specimens or quality control samples.

The kit contains the following:

Xpert TV Assay cartridges with integrated reaction tubes	**10**
• Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
• Lysis Reagent (Guanidinium thiocyanate)	1.6 mL per cartridge
• Sodium Hydroxide	0.4 mL per cartridge
• Wash Reagent	0.5 mL per cartridge
• Elution Reagent	2.0 mL per cartridge
• Binding Reagent	1.5 mL per cartridge
Transfer Pipettes (500 µL)	**10**
CD	**1**
• Assay Definition File (ADF)	
• Instructions to import ADF into GeneXpert software	
• Instructions for Use (Package Insert)	

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

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

6.2 Storage and Handling

- Store the Xpert TV Assay cartridges at 2–28°C.
- Do not open a cartridge until ready to perform testing.
- Use cartridges within 30 minutes after opening the cartridge lid.
- Do not use cartridges that have passed the expiration date.
- Do not use a cartridge that has leaked.
- Do not use any reagents that have become cloudy or discolored.

6.3 Materials Required but Not Provided

- Primary samples must be collected and treated with the appropriate kit:
  - URINE/A-50: Xpert Urine Specimen Collection Kit
  - SWAB/A-50: Xpert Vaginal/Endocervical Swab Specimen Collection Kit
- SWAB/G-50: Xpert Swab Specimen Collection Kit
- GeneXpert Dx Instrument or GeneXpert Infinity Systems (catalog number varies by configuration): GeneXpert instrument, computer, barcode scanner, Operator Manual.
  - For GeneXpert Dx System: GeneXpert Dx software version 4.3 or higher

Note Use this product with GeneXpert Software Version 4.3 or higher

6.4 Materials Available but Not Provided

- Printer (If a printer is required, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.)

7 Warnings and Precautions

7.1 General

- For *in vitro* diagnostic use.
- For prescription use only.
- 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[4] and the Clinical and Laboratory Standards Institute.[5]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Good laboratory practices and changing gloves between handling patient specimens are recommended to avoid contamination of specimens.

7.2 Specimen Collection

- For collection of endocervical swab specimens and patient-collected vaginal swab specimens, use only the Xpert Vaginal/ Endocervical Specimen Collection Kit or Xpert Swab Specimen Collection Kit.
- For collection of urine specimens, use only the Xpert Urine Specimen Collection Kit with unpreserved (neat), first-catch urine.
- Under or over dispensing of urine into the Xpert Urine Transport Reagent tubes may affect assay performance.
- Endocervical and patient-collected vaginal swab specimens must be collected and tested before the expiration date of the Xpert Swab Transport Reagent.
- Urine specimens must be collected and tested before the expiration date of the Xpert Urine Transport Reagent.

7.3 Assay Reagent

- Do not substitute Xpert TV Assay reagents with other reagents.
- Do not open the Xpert TV Assay cartridge lid until you are ready to add a sample during testing.
- 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 TV Assay cartridge is used to process one test. Do not reuse processed cartridges.
- Each single-use disposable pipette is used to transfer one specimen. Do not use disposable pipettes more than one time.
- Do not test the endocervical or patient-collected vaginal specimens received in the laboratory without the swab present. A false negative test result may occur.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- CHANGE GLOVES if they come in contact with specimen or appear to be wet to avoid contaminating other specimens. Change gloves before leaving work area and upon entry into work area.
- Wear clean lab coats and gloves. Change gloves between processing each sample.
- In the event of a spill of specimens or controls, wear gloves and absorb the spill with paper towels. Then, thoroughly clean the contaminated area with a 1:10 dilution of freshly prepared household chlorine bleach. Final active chlorine concentration should be 0.5% regardless of the household bleach concentration in your country. Allow a minimum of two minutes contact time. Ensure the work area is dry before using 70% denatured ethanol to remove bleach residue. Allow surface to dry completely before proceeding. Or, follow your institution's standard procedures for a contamination or spill event. For equipment, follow the manufacturer's recommendations for decontamination of equipment.
- Biological specimens, transfer devices and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedure 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.[6]

8 Chemical Hazards[7, 8]

UN GHS Hazard Pictogram: 
Signal word: WARNING

- **UN GHS Hazard Statements**
  - May be harmful if swallowed
  - Causes mild skin irritation
  - Causes serious eye irritation
- **UN GHS Precautionary Statements**
  - **Prevention**
    - Wash thoroughly after handling.
    - Wear protective gloves/protective clothing/eye protection/face protection.
  - **Response**
    - Call a POISION CENTER or doctor/physician if you feel unwell.
    - If skin irritation occurs: Get medical advice/attention.
    - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
    - If eye irritation persist: Get medical advice/attention.

9 Specimen Transport and Storage

- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen. Specimen stability under shipping conditions other than those recommended has not been evaluated.

Refer to the appropriate specimen collection kit package insert for collection and transport instructions.

Important **Failure to store specimens as outlined in Table 1 through Table 3 may cause false negative results.**

Table 1. Unprocessed Urine Specimen

Specimen	Transport and Storage Temperature (°C)	Storage Time
Female and Male Urine	2–8 °C	4 days
	15–30 °C	4 hours

Table 2. Urine Specimens in Xpert Urine Transport Reagent

Specimen	Transport and Storage Temperature (°C)	Storage Time
Female and Male Urine in Xpert Urine Transport Reagent	2–8 °C	28 days
	15–30 °C	14 days

Table 3. Swab Specimens in Xpert Swab Transport Reagent

Specimen	Transport and Storage Temperature (°C)	Storage Time
Endocervical Swab in Xpert Swab Transport Reagent	2–30 °C	60 days
Vaginal Swab in Xpert Swab Transport Reagent	2–30 °C	60 days

10 Procedure

Before starting these procedures, make sure that the GeneXpert instrument is running with GeneXpert Dx software version 4.3 or higher or Xpertise software.

Important **Start the test within 30 minutes of opening the cartridge lid.**

10.1 Preparing the Cartridge

To add the sample to the Xpert TV Assay cartridge:

1. Obtain the following items:
   - Xpert TV Assay cartridge
   - Transfer pipette (provided). Line on pipette indicates 500 µL fill volume.
   - Appropriately collected and labeled test sample in the Xpert Specimen Collection Kit transport reagent tube.
2. Inspect the test cartridge for damage. If damaged, do not use it.
3. Open the cartridge lid.
4. Gently invert the transport tube three to four times to ensure adequate mixing of sample and transport reagent.
5. Unwrap the transfer pipette.
6. Remove the transport tube cap, compress the bulb of the transfer pipette, insert the pipette into the transport tube and release the bulb to fill the transfer pipette up to the mark (500 µL) on the pipette shaft. See Figure 1. Ensure the pipette is filled with no air bubbles present.

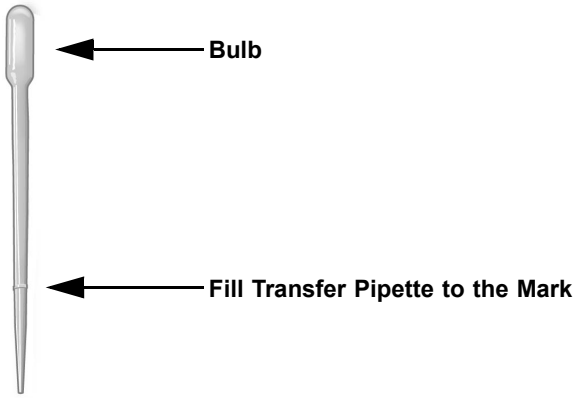

Figure 1. Transfer Pipette and Fill Mark

7. Empty the pipette's contents into the sample chamber of the cartridge. See Figure 2. Retain the remaining sample according to the conditions described in Table 2 and Table 3 in case a retest is required.

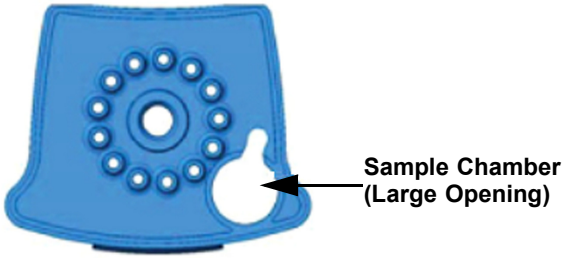

Figure 2. Xpert TV Assay Cartridge (Top View)

8. Close the cartridge lid.

10.2 Starting the Test

Important **Before you start the test, make sure the system is running GeneXpert 4.3 software or higher and that the Xpert TV Assay Definition File (ADF) is imported into the software. This section lists the basic steps of running the test. For detailed instructions, see the GeneXpert Dx System Operator Manual or the GeneXpert Infinity System Operator Manual, depending on the model that is being used.**

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

1. Turn on the GeneXpert instrument:
   - If using the GeneXpert Dx instrument, first turn on the instrument, and then turn on the computer. The GeneXpert software will launch automatically or may require double-clicking the GeneXpert Dx software icon on the Windows® desktop.

     Or

   - If using the GeneXpert Infinity instrument, power up the instrument. The GeneXpert software will launch automatically or may require double-clicking the Xpertise software icon on the Windows desktop.
2. Log on to the GeneXpert Instrument System software using your user name and password.
3. In the GeneXpert System window, click **Create Test** (GeneXpert Dx) or click **Orders** and **Order Test** (Infinity). The **Create Test** window and Scan Patient ID Barcode dialog box appears.
4. Scan or type in the Patient ID (optional). If typing the Patient ID, make sure the Patient ID is typed correctly. The Patient ID is shown on the left side of the View Results window and is associated with the test results. The Scan Sample ID dialog box appears.
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 shown on the left side of the View Results window and in all reports. The Scan Cartridge dialog box appears.
6. Scan the barcode on the Xpert TV Assay cartridge. The Create Test window is displayed showing the information entered. 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 Xpert TV Assay cartridge does not scan, then repeat the test with a new cartridge. See Section 13.2, Retest Procedure.

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. Then remove the cartridge.
   D. The used cartridges should be disposed in the appropriate specimen waste container according to your institution's standard practices.

10.3 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 G*eneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

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

11 Quality Control

11.1 Built-in Quality Controls

CONTROL

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

- **Sample Processing Control (SPC):** Ensures the sample was correctly processed. The SPC contains genomic DNA of *Bacillus globigii* that is included in each cartridge to verify adequate processing of the sample. The SPC verifies that binding and elution of *Trichomonas vaginalis* target DNA has occurred if the organism is present and verifies that the sample processing is adequate. Additionally, this control detects sample-associated inhibition of the real-time PCR assay. The SPC should be positive in an analyte negative sample and can be negative or positive in an analyte positive sample. The SPC passes if it meets the validated acceptance criteria.
- **Sample Adequacy Control (SAC):** Verifies that the sample contains human cells or human DNA. This multiplex assay includes primers and probes for the detection of a single copy human gene. The SAC signal is only to be considered in an analyte negative sample. A negative SAC indicates that no human cells are present in the sample due to insufficient mixing of the sample or because of an inadequately collected sample.
- **Probe Check Control (PCC)**: Before the start of the PCR reaction, the GeneXpert 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.

11.2 External Controls

Positive and negative external controls should be used in accordance with local, state, and federal accrediting organizations' requirements as applicable.

12 Interpretation of Results

The results are interpreted automatically by the GeneXpert Instrument System from measured fluorescent signals and embedded calculation algorithms. Results are clearly shown on the Test Result tab of the View Results window.

All possible Xpert TV Assay results and their interpretation are shown in Table 4. See Figure 3, Figure 4, Figure 5, and Figure 6 for specific examples of these test results.

Table 4. Xpert TV Assay Results and Interpretation

Result	Interpretation
TV DETECTED (See Figure 3 and Figure 4.)	*Trichomonas* target DNA is detected. • The *Trichomonas* target has a Ct within the valid range and a fluorescence endpoint above the threshold setting. • SPC – Not applicable. SPC is ignored because the *Trichomonas* target amplification may compete with this control. • SAC – Not applicable. SAC is ignored because the *Trichomonas* target amplification may compete with this control. • PCC – PASS. All probe check results pass.
TV NOT DETECTED (See Figure 5.)	*Trichomonas* target DNA is not detected. SPC meets acceptance criteria. • *Trichomonas* target DNA is not detected. • SPC – PASS. SPC has a Ct within the valid range and fluorescence endpoint above the threshold setting. • SAC – PASS. SAC has a Ct within the valid range and a fluorescence endpoint above the threshold setting. • PCC – PASS. All probe check results pass.

Table 4. Xpert TV Assay Results and Interpretation (Continued)

Result	Interpretation
INVALID (See Figure 6.)	Presence or absence of *Trichomonas* target DNA cannot be determined. Repeat test according to the instructions in Section 13.2, Retest Procedure. • SPC – FAIL. SPC Ct is not within valid range and the fluorescence endpoint is below the threshold setting. • SAC – PASS. SAC has a Ct within the valid range and fluorescence endpoint in the above threshold setting. • PCC – PASS. All probe check results pass. *Or* • SPC – PASS. SPC has a Ct within the valid range and fluorescence endpoint above the threshold setting. • SAC – FAIL. SAC Ct is not within valid range and fluorescence endpoint is below the threshold setting. • PCC – PASS. All probe check results pass. *Or* • SPC – FAIL. SPC Ct is not within valid range and fluorescence endpoint is below the threshold setting. • SAC – FAIL. SAC Ct is not within valid range and fluorescence endpoint is below the threshold setting. • PCC – PASS. All probe check results pass.
ERROR	Presence or absence of *Trichomonas* target DNA cannot be determined. Repeat test according to the instructions in Section 13.2, Retest Procedure. • TRICHOMONAS – NO RESULT • SPC – NO RESULT • 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 *Trichomonas* target DNA cannot be determined. Repeat test according to the instructions in Section 13.2, 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. • TRICHOMONAS – NO RESULT • SPC – NO RESULT • SAC – NO RESULT • PCC – Not applicable

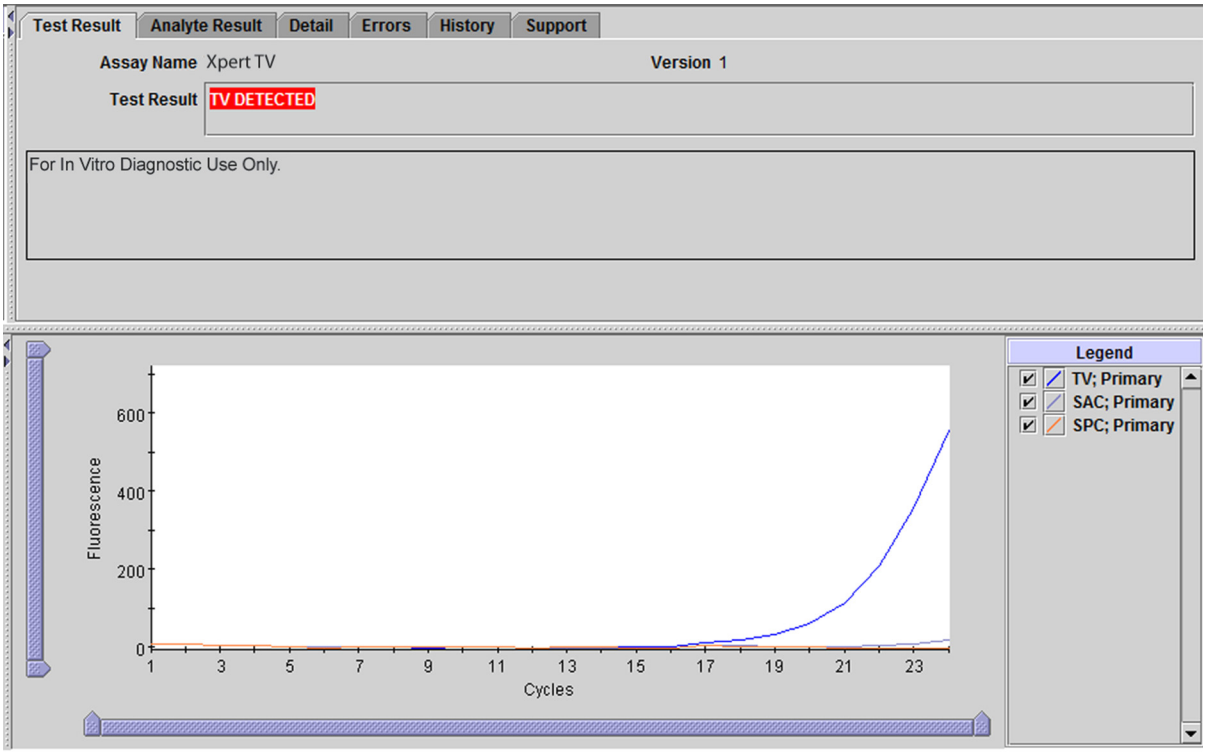

Figure 3. An Example of Xpert TV Assay - TV DETECTED Early Assay Termination

Note The Early Assay Termination function shown in Figure 3 delivers positive results as soon as the target DNA reaches the predetermined threshold.

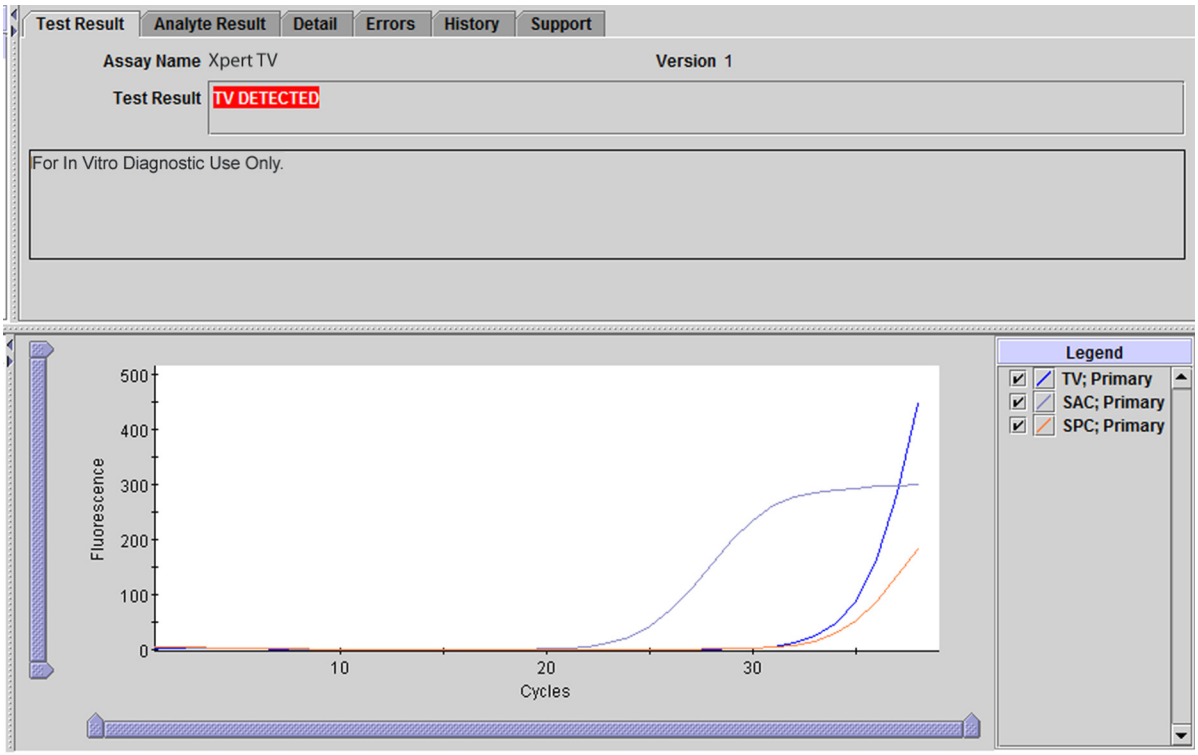

Figure 4. An Example of Xpert TV Assay - TV DETECTED

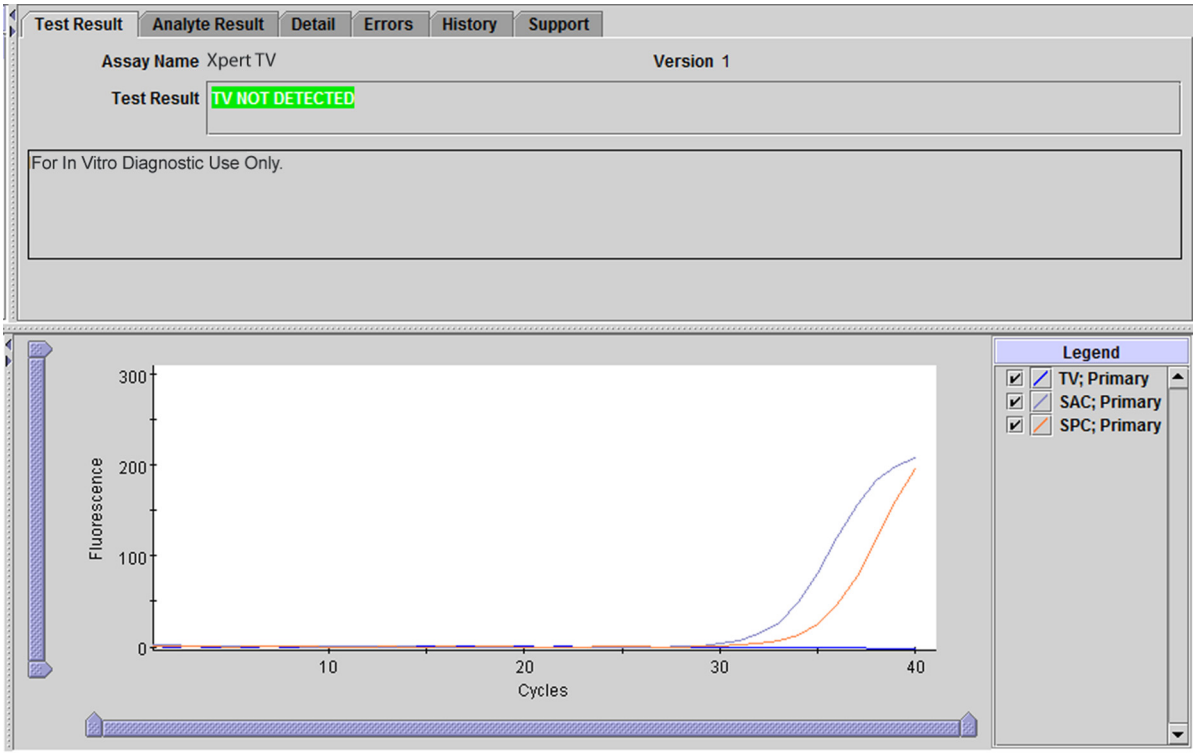

Figure 5. An Example of Xpert TV Assay - TV NOT DETECTED

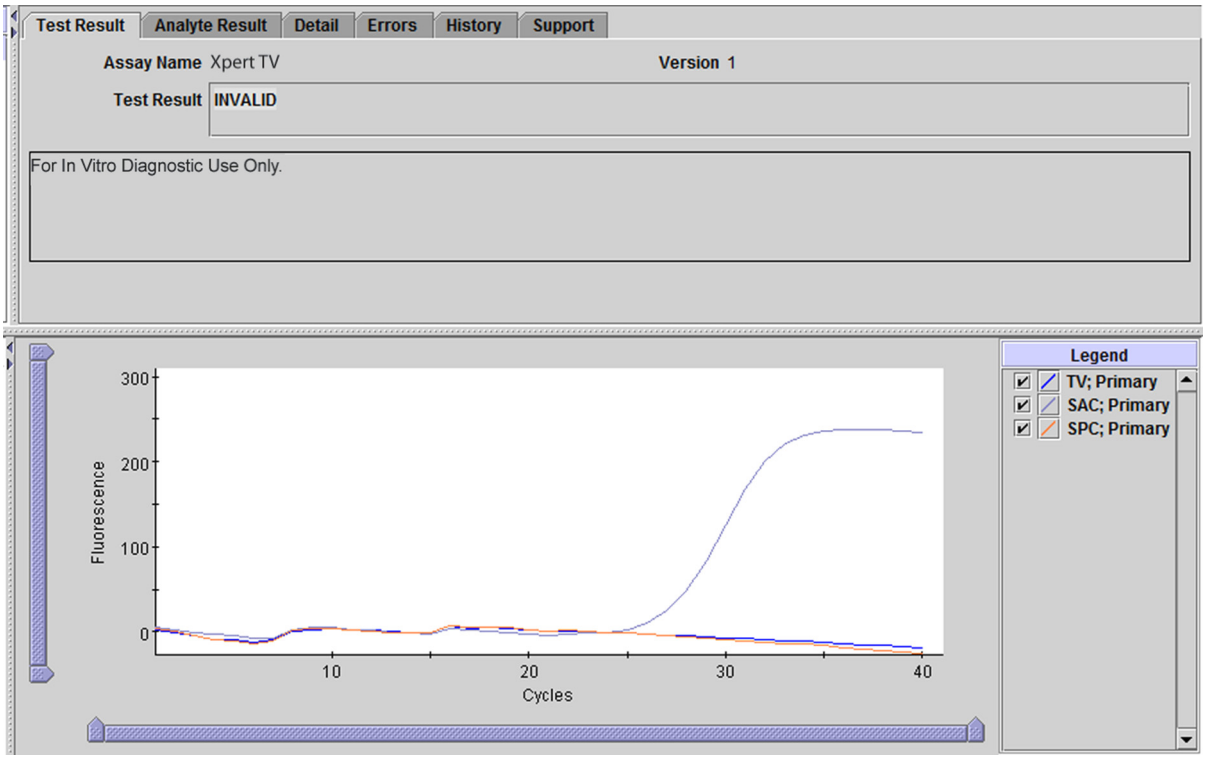

Figure 6. An Example of an INVALID Result

13 Retests

13.1 Reasons to Repeat the Assay

- If any of the following test results occur, repeat the test according to instructions in the Retest Procedure. Repeat the test using a new cartridge (do not re-use the cartridge).
- An **INVALID** result indicates that the SPC and/or the SAC failed. The sample was not properly processed, PCR was inhibited or the sample was not properly collected.
- An **ERROR** result indicates that the test failed possibly because the reaction tube was filled improperly, a reagent probe integrity problem was detected, pressure limits were exceeded, or a valve positioning error was detected.
- 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.

13.2 Retest Procedure

- Obtain the leftover sample from the Xpert Swab Transport Reagent Tube or Xpert Urine Transport Reagent Tube. Repeat the test with a new cartridge (do not re-use the cartridge). See 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.

14 Limitations

- The Xpert TV Assay has only been validated with the following specimen types, collected with the Xpert Vaginal/ Endocervical Specimen Collection Kit, Xpert Swab Specimen Collection Kit, or the Xpert Urine Specimen Collection Kit:
  - Endocervical swabs
  - Patient-collected vaginal swabs
  - Female and male first-catch urine
- A negative test result does not exclude the possibility of infection because test results may be affected by improper specimen collection, technical error, sample mix-up, or because the number of organisms in the sample is below the limit of detection of the test.
- Careful compliance with the instructions in this package insert and in the Xpert Vaginal/Endocervical Specimen Collection Kit, Xpert Swab Specimen Collection Kit, and Xpert Urine Specimen Collection Kit package inserts is necessary to avoid erroneous results.
- The Xpert TV Assay has been validated using the procedures provided in this package insert only. Modifications to these procedures may alter the performance of the test.
- Because the detection of *Trichomonas vaginalis* is dependent on the organism's DNA present in the sample, reliable results are dependent on proper sample collection, handling, and storage.
- *Trichomonas tenax* was found to cross-react with the Xpert TV Assay at levels above 1.0×10^2 cells/mL. *T. tenax* is a commensal of the oral cavity. See Xpert TV Analytical Specificity for details.
- With endocervical and patient-collected vaginal specimens, assay interference may be observed in the presence of blood (>60% v/v).
- As with many diagnostic tests, results from the Xpert TV Assay should be interpreted in conjunction with other laboratory and clinical data available to the clinician.
- The patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated.
- The Xpert TV Assay has not been validated for use with vaginal swab specimens collected by patients at home. The patient collected vaginal swab specimen application is limited to healthcare facilities where support/counseling is available to explain procedures and precautions.
- The Xpert TV Assay provides qualitative results. No correlation can be drawn between the magnitude of the Ct value and the number of cells in an infected sample.
- The Xpert TV Assay should not be used for the evaluation of suspected sexual abuse or for other medico-legal indications.
- The predictive value of an assay depends on the prevalence of the disease in any particular population. See Table 5 for hypothetical predictive values when testing varied populations.
- Mutations or nucleotide polymorphisms in primer or probe binding regions may affect detection of new or unknown *Trichomonas vaginalis* variants resulting in a false negative result.
- Xpert TV Assay performance has not been evaluated in pregnant women, or in patients with a history of hysterectomy.

- Xpert TV Assay performance has not been evaluated in patients less than 18 years of age or older than 78 years of age.

15 Expected Values

The prevalence of infection with *Trichomonas vaginalis* in patient populations depends on risk factors such as age, gender, the presence or absence of symptoms, the type of clinic, and the sensitivity of the test used to detect infections. During the clinical evaluation of the Xpert TV Assay, the observed *Trichomonas vaginalis* prevalence rate in females was 10.3% and in males was 3.1%.

The estimated positive predictive value (PPV) and negative predictive value (NPV) of the Xpert TV Assay across different hypothetical prevalence rates are shown for each specimen type in Table 5. These calculations are based on the overall estimated sensitivity and specificity observed for each specimen type during the Xpert TV multi-center clinical study (Table 6).

The overall sensitivity and specificity for male urine (UR-M) were 97.2% and 99.9%, respectively. The overall sensitivity and specificity for female urine (UR-F) were 100% and 99.7%, respectively. In patient-collected vaginal swab specimens (PC-VS), the overall sensitivity and specificity were 98.5% and 99.9%, respectively. For endocervical swabs (ES), the overall sensitivity and specificity were 99.5% and 99.4%, respectively.

Table 5. Hypothetical PPV and NPV of the Xpert TV Assay by Specimen Type

Specimen Type	Prevalence (%)	PPV (%)	NPV (%)
Male UR	1	91.6%	100.0%
	2	95.7%	99.9%
	5	98.3%	99.9%
	10	99.2%	99.7%
	12	99.3%	99.6%
	15	99.5%	99.5%
	20	99.6%	99.3%
	25	99.7%	99.1%
Female UR	1	76.5%	100.0%
	2	86.8%	100.0%
	5	94.4%	100.0%
	10	97.3%	100.0%
	12	97.8%	100.0%
	15	98.3%	100.0%
	20	98.8%	100.0%
	25	99.1%	100.0%

Table 5. Hypothetical PPV and NPV of the Xpert TV Assay by Specimen Type (Continued)

Specimen Type	Prevalence (%)	PPV (%)	NPV (%)
PC-VS	1	88.8%	100.0%
	2	94.1%	100.0%
	5	97.6%	99.9%
	10	98.9%	99.8%
	12	99.1%	99.8%
	15	99.3%	99.7%
	20	99.5%	99.6%
	25	99.6%	99.5%
ES	1	61.9%	100.0%
	2	76.6%	100.0%
	5	89.4%	100.0%
	10	94.7%	99.9%
	12	95.6%	99.9%
	15	96.6%	99.9%
	20	97.6%	99.9%
	25	98.2%	99.8%

16 Performance Characteristics

16.1 Clinical Performance

Performance characteristics of the Xpert TV Assay were determined in a multi-site prospective investigational study by comparing the results from the Xpert TV Assay to a patient infected status (PIS) algorithm comprised of culture and validated bi-directional sequencing (primary sequencing) for male urine, or an FDA cleared NAAT test and culture for female specimen types.

Study participants included consenting asymptomatic and symptomatic, sexually active males and females seen at locations including, but not limited to: OB/GYN, sexually transmitted disease (STD), and family planning clinics. The average age among eligible female study participants was 33.5 years (range = 18 to 78 years). The average age among eligible male study participants was 36.2 years (range = 16 to 78 years).

The study specimens consisted of prospectively collected male urine, female urine, endocervical swabs, and patient-collected vaginal swabs (collected in a clinical setting). Clinician-collected vaginal swabs were collected for testing by the reference NAAT test and culture. Samples were collected from 17 clinical sites and tested at 11 sites. Reference testing was performed at 3 central laboratories.

A study participant was considered to be infected by PIS if either of the two reference test results were positive. The subject was considered to be not infected by PIS when both reference test results were negative.

Performance of the Xpert TV Assay was calculated relative to the PIS for each of the three female specimen types (endocervical swabs, patient-collected vaginal swabs and urine) or to the PIS for male urine, respectively.

Specimens with discrepant results between the Xpert TV Assay and the PIS were analyzed by validated bi-directional Sanger sequencing and results are reflected in Table 6.

Among the 10,017 tests performed, 190 had initial ERROR, INVALID, or NO RESULT outcomes (1.90%, 95% CI 1.65-2.18). Of those, 167 specimens yielded valid results upon repeat assay (7 specimens were not retested). The overall valid reporting rate of the assay was 99.8% (9994/10,017).

Results of the Xpert TV Assay were compared to the PIS and discrepant sequencing for determination of sensitivity, specificity, and predictive values. Sensitivity and specificity for TV by specimen type and symptom status are presented in Table 6.

Table 6. Xpert TV vs. PIS with Discrepant Sequencing by Symptomatic Status

Sample Type	Status	Total (n)	Sens	95% CI	Spec	95% CI	Prev (%)	PPV (%)	NPV (%)
ES	Symp	685	100% (75/75)	95.1%-100%	99.2% (605/610)	98.1%-99.6%	10.9%	93.8%	100%
	Asymp	1114	99.1% (108/109)	95.0%-99.8%	99.5% (1000/1005)	98.8%-99.8%	9.8%	95.6%	99.9%
	Overall	1799	99.5% (183/184)	97.0%-99.9%	99.4% (1605/1615)	98.9%-99.7%	10.2%	94.8%	99.9%
	Difference	P-Value	P=1.000	-0.87%, 2.71%	P=0.517	-1.16%, 0.52%			
PC-VS	Symp	682	100% (75/75)	95.1%-100%	99.8% (606/607)	99.1%-100%	11.0%	98.7%	100%
	Asymp	1109	97.5% (116/119)	92.9%-99.1%	99.9% (989/990)	99.4%-100%	10.7%	99.1%	99.7%
	Overall	1791	98.5% (191/194)	95.6%-99.5%	99.9% (1595/1597)	99.5%-100%	10.8%	99.0%	99.8%
	Difference	P-Value	P=0.285	-0.30%, 5.34%	P=1.000	-0.44%, 0.31%			
UR-F	Symp	688	100% (71/71)	94.9%-100%	99.8% (616/617)	99.1%-100%	10.3%	98.6%	100%
	Asymp	1105	100% (109/109)	96.6%-100%	99.6% (992/996)	99.0.%-99.8%	9.9%	96.5%	100%
	Overall	1793	100% (180/180)	97.9%-100%	99.7% (1608/1613)	99.3%-99.9%	10.0%	97.3%	100%
	Difference	P-Value	P=1.000	NA	P=0.655	-0.27%, 0.74%			
UR-M	Symp	1088	96.8% (30/31)	83.8%-99.4%	100% (1057/1057)	99.6%-100%	2.8%	100%	99.9%
	Asymp	3523	97.3% (109/112)	92.4%-99.1%	99.9% (3407/3411)	99.7%-100%	3.2%	96.5%	99.9%
	Overall	4611	97.2% (139/143)	93.0%-98.9%	99.9% (4464/4468)	99.8%-100%	3.1%	97.2%	99.9%
	Difference	P-Value	P=1.000	-7.5%, 6.4%	P=0.579	0.00%, 0.23%			

ES=endocervical swab, PC-VS=patient-collected vaginal swab, UR-F= female urine, UR-M= male urine

Cycle Threshold (Ct) Frequency Distribution

Patient-collected vaginal swabs, endocervical swabs and urine specimens were collected from 1867 females and urine specimens were collected from 4626 males at 17 collection sites in the US. The frequency distribution of Xpert TV Assay positive results for the 197 *Trichomonas vaginalis* infected female study subjects and 125 *Trichomonas vaginalis* infected male study subjects are shown in Figure 7.

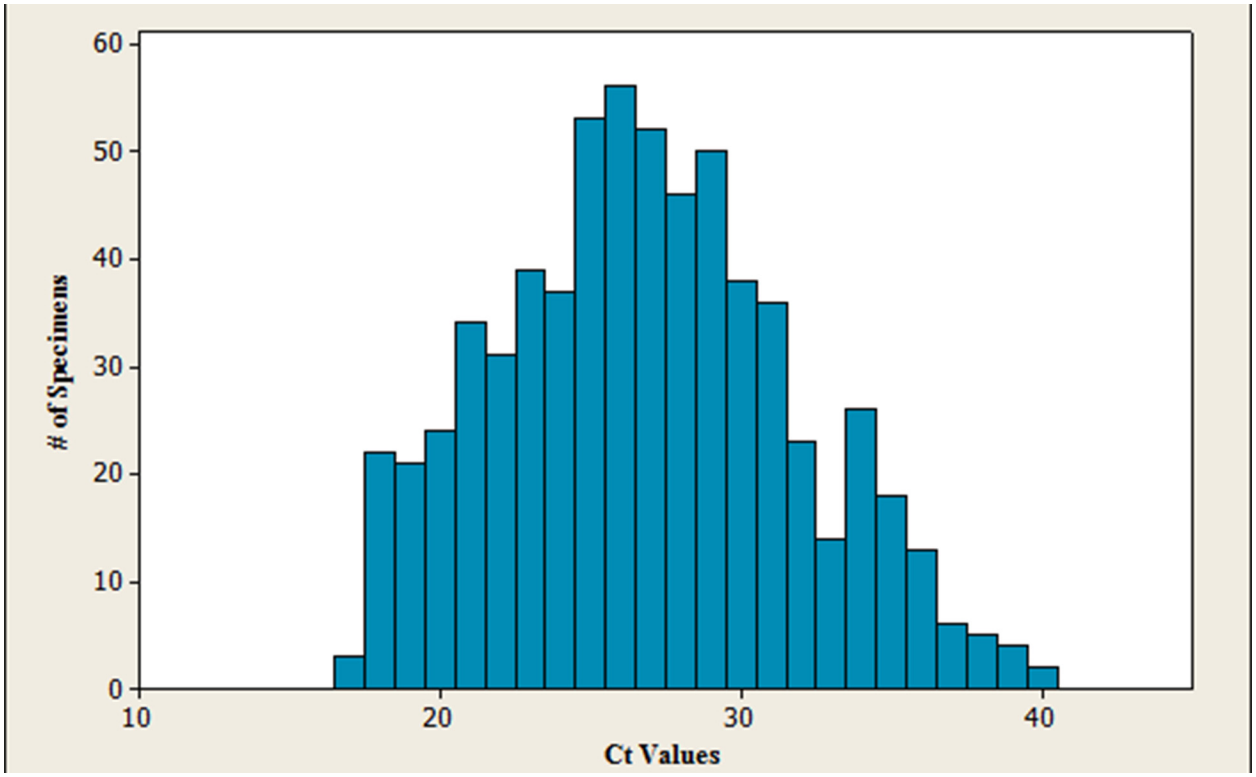

Figure 7. Ct Distribution of Patients Designated as Positive for TV Based on PIS Algorithm

17 Analytical Performance

17.1 Analytical Sensitivity (Limit of Detection)

The analytical sensitivity or limit of detection (LoD) of the Xpert TV Assay was assessed using two *Trichomonas vaginalis* strains, one metronidazole susceptible (*T. vaginalis* ATCC® 30001™), and one metronidazole resistant (*T. vaginalis* ATCC® 30238™). The strains were tested individually in clinical *T. vaginalis*-negative pooled urine matrix in Cepheid Xpert Urine Transport Reagent and clinical *T. vaginalis*-negative pooled vaginal swab matrix (VS) in Cepheid Xpert Swab Transport Reagent.

T. vaginalis was cultured and incubated at 35°C. Visual examination of the cultures for white precipitate (indicating growth) was conducted every 24 hours for 3 to 5 days. Cell pellets were resuspended in growth medium and enumerated visually using light microscopy. The concentration of isolates was expressed as the number of cells per milliliter (cells/mL). Cultures were diluted in culture medium to 1 x10^4 cells/mL and stored at -20°C. Cells were thawed on ice for use in the study.

The LoD was estimated by testing replicates of 20 at five concentrations for each strain and sample type over three days. The LoD for each strain was estimated by probit analysis. The claimed LoDs were confirmed by analyzing at least 20 replicates with *T. vaginalis* cells diluted to the estimated LoD concentrations. The LoD is defined as the lowest number of cells/mL that can be reproducibly distinguished from negative samples with 95% confidence or the lowest concentration at which 19 of 20 replicates were positive. The study was performed with two different lots of Xpert TV reagents and the claimed LoD for each strain is the higher of the two determinations (Table 7). The claimed LoD for *T. vaginalis* strains ATCC 30001 and ATCC 30238 in vaginal swab matrix is 2 cells/mL. The claimed LoD for *T. vaginalis* strain ATCC 30001 in urine matrix is 3 cells/mL. The claimed LoD for *T. vaginalis* strain ATCC 30238 in urine matrix is 2 cells/mL.

Table 7. LoD of Two *T. vaginalis* Strains in Pooled Vaginal Swab Matrix and Urine Matrix

Trichomonas vaginalis strain and matrix	LoD Estimates by Probit Analysis (cells/mL)		Verified LoD (cells/mL)	Verification (Positives/20)	Mean TV Ct	Mean SAC Ct	Mean SPC Ct	LoD Claim (cells/mL)
	Reagent Lot 1	Reagent Lot 2						
ATCC 30001 in Vaginal Swab	2.0	1.6	2.0	20/20	39.1	21.4	33.9	2
ATCC 30238 in Vaginal Swab	1.7	2.1	2.1	20/20	37.5	21.4	33.7	2
ATCC 30001 in Urine	2.2	2.5	2.5	20/20	38.2	29.3	34.1	3
ATCC 30238 in Urine	2.1	1.7	2.1	20/20	38.2	29.2	33.8	2

17.2 Analytical Reactivity (Inclusivity)

The analytical inclusivity of the Xpert TV Assay was evaluated by testing 17 *T. vaginalis* strains diluted in either negative pooled vaginal swab matrix in Cepheid Xpert Swab Transport Reagent or negative pooled urine in Cepheid Xpert Urine Transport Reagent. All *T. vaginalis* strains were tested in triplicate at a concentration of 3X the analytical LoD for the respective specimen type (6 cells/mL for vaginal swabs and 7.5 cells/mL for urine). All strains tested were reported as **TV DETECTED**. Results are shown in Table 8. Positive and negative controls were included in the study. The inclusivity for the 17 *T. vaginalis* strains tested was 100%.

Table 8. Analytical Reactivity (Inclusivity) of Xpert TV Assay

Isolate ATCC #	Isolation Source	Results Vaginal Swab	Results Urine
30001	Vaginal exudate	TV DETECTED	TV DETECTED
30184	Vaginal swab	TV DETECTED	TV DETECTED
30187	Endocervical swab	TV DETECTED	TV DETECTED
30188	Vagina	TV DETECTED	TV DETECTED
30236	Endocervical swab	TV DETECTED	TV DETECTED
30240	Vaginal pool	TV DETECTED	TV DETECTED
30245	Vaginal and Endocervical material	TV DETECTED	TV DETECTED
30247	Vagina	TV DETECTED	TV DETECTED
50138	human	TV DETECTED	TV DETECTED
50139	human	TV DETECTED	TV DETECTED
50141	human	TV DETECTED	TV DETECTED
50143	human	TV DETECTED	TV DETECTED
50147	human	TV DETECTED	TV DETECTED
50167	Vagina	TV DETECTED	TV DETECTED
50183	Prostatic fluid	TV DETECTED	TV DETECTED
PRA-95	Vaginal exudate	TV DETECTED	TV DETECTED
PRA-98	human	TV DETECTED	TV DETECTED

17.3 Analytical Specificity (Cross-Reactivity and Competitive Interference)

A panel of 124 microorganisms, including bacteria, fungi, and viruses commonly found in the urogenital tract, as well as other protozoans closely related to *T. vaginalis* were tested with the Xpert TV Assay. The microorganisms were tested in the presence (competitive interference) and absence (cross-reactivity) of 3X LoD *T. vaginalis* ATCC 30001 cells. The microorganisms were seeded into either pooled *Trichomonas vaginalis*-negative urine matrix (patient urine added to Cepheid Urine Transport Reagent) or pooled *Trichomonas vaginalis*-negative vaginal swab matrix (vaginal swabs collected into Cepheid Swab Transport Reagent).

Each bacterial or fungal strain was tested at 1 x 106 CFU/mL or greater or at 1 x 10^6 genomes/mL. Viral strains were tested at 1 x 105 $TCID_{50}$/mL or 105 genomes/mL or greater. Protozoans were cultured in growth media, visually enumerated by light microscopy and tested at 1 x 105 cells/mL or greater or 105 genomes/mL. All microorganisms were tested in triplicate. Positive and negative controls were included in the study. One organism, *Trichomonas tenax*, demonstrated cross-reactivity (result of **TV DETECTED** in the absence of TV) at 1 x 10^5 cells/mL for the urine and vaginal swab matrix samples. *Trichomonas tenax* was subjected to repeat analysis at various other concentrations until a result of **TV NOT DETECTED** was obtained (at 1 x 10^2 cells/mL). This is addressed in Section 14, Limitations. For the other 123 microorganisms, all TV positive samples remained positive and all TV negative samples remained negative, indicating that there was no interference or cross-reactivity with the results of the Xpert TV Assay for these microorganisms. Results are shown in Table 9 and Table 10 for urine and vaginal swab matrix, respectively.

Table 9. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Urine Matrix

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Achromobacter xerosis	8 x 10^6	TV NOT DETECTED	TV DETECTED
Acinetobacter calcoaceticus	3 x 10^6	TV NOT DETECTED	TV DETECTED
Acinetobacter lwoffii	6 x 10^6	TV NOT DETECTED	TV DETECTED
Actinomyces israelii[b]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Actinomyces pyogenes	8 x 10^6	TV NOT DETECTED	TV DETECTED
Aerococcus viridans	5 x 10^6	TV NOT DETECTED	TV DETECTED
Aeromonas hydrophila	1 x 10^7	TV NOT DETECTED	TV DETECTED
Alcaligenes faecalis	1 x 10^7	TV NOT DETECTED	TV DETECTED
Atopobium vaginae[b]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Bacillus subtilis	6 x 10^6	TV NOT DETECTED	TV DETECTED
Bacteroides fragilis[b]	5 x 10^6	TV NOT DETECTED	TV DETECTED
Bacteroides ureolyticus[b]	1 x 10^6	TV NOT DETECTED	TV DETECTED
Bifidobacterium adolescentis[b]	6 x 10^6	TV NOT DETECTED	TV DETECTED
Bifidobacterium brevi (breve)[b]	9 x 10^6	TV NOT DETECTED	TV DETECTED
Blastocystis hominis[c]	1 x 10^{5d}	TV NOT DETECTED	TV DETECTED
Branhamella catarrhalis	1 x 10^7	TV NOT DETECTED	TV DETECTED
Brevibacterium linens	7 x 10^6	TV NOT DETECTED	TV DETECTED
Campylobacter jejuni	1 x 10^7	TV NOT DETECTED	TV DETECTED
Candida albicans[e]	7 x 10^6	TV NOT DETECTED	TV DETECTED
Candida glabrata[e]	4 x 10^6	TV NOT DETECTED	TV DETECTED
Candida parapsilosi[e]	7 x 10^6	TV NOT DETECTED	TV DETECTED
Candida tropicalis[e]	6 x 10^6	TV NOT DETECTED	TV DETECTED
Chlamydia trachomatis	2 x 10^6	TV NOT DETECTED	TV DETECTED
Chromobacterium violaceum	7 x 10^6	TV NOT DETECTED	TV DETECTED
Citrobacter freundii	1 x 10^6	TV NOT DETECTED	TV DETECTED

Table 9. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Urine Matrix (Continued)

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Clostridium difficile[b]	4×10^6	TV NOT DETECTED	TV DETECTED
Clostridium perfringens[b]	2×10^6	TV NOT DETECTED	TV DETECTED
Corynebacterium genitalium	2×10^6	TV NOT DETECTED	TV DETECTED
Corynebacterium xerosis	3×10^6	TV NOT DETECTED	TV DETECTED
Cryptococcus neoformans[e]	6×10^6	TV NOT DETECTED	TV DETECTED
Cryptosporidium parvum[c]	1×10^{5d}	TV NOT DETECTED	TV DETECTED
Cytomegalovirus[f]	5×10^5	TV NOT DETECTED	TV DETECTED
Deinococcus radiodurans	5×10^6	TV NOT DETECTED	TV DETECTED
Derxia gummosa	1×10^{6d}	TV NOT DETECTED	TV DETECTED
Eikenella corrodens	5×10^6	TV NOT DETECTED	TV DETECTED
Entamoeba histolytica[c]	1×10^{5d}	TV NOT DETECTED	TV DETECTED
Enterobacter aerogenes	1×10^6	TV NOT DETECTED	TV DETECTED
Enterobacter cloacae	2×10^6	TV NOT DETECTED	TV DETECTED
Enterococcus avium	7×10^6	TV NOT DETECTED	TV DETECTED
Enterococcus faecalis	7×10^6	TV NOT DETECTED	TV DETECTED
Enterococcus faecium	4×10^6	TV NOT DETECTED	TV DETECTED
Erysipelothrix rhusiopathiae	1×10^7	TV NOT DETECTED	TV DETECTED
Escherichia coli	1×10^7	TV NOT DETECTED	TV DETECTED
Flavobacterium meningosepticum	1×10^7	TV NOT DETECTED	TV DETECTED
Fusobacterium nucleatum[b]	4×10^6	TV NOT DETECTED	TV DETECTED
Gardnerella vaginalis	2×10^6	TV NOT DETECTED	TV DETECTED
Gemella haemolysans	6×10^6	TV NOT DETECTED	TV DETECTED
Giardia intestinalis[c]	1×10^{5d}	TV NOT DETECTED	TV DETECTED
Haemophilus ducreyi	1×10^{6d}	TV NOT DETECTED	TV DETECTED
Haemophilus influenzae	3×10^6	TV NOT DETECTED	TV DETECTED
Herpes simplex virus I[f]	1×10^5	TV NOT DETECTED	TV DETECTED
Herpes simplex virus II[f]	1×10^5	TV NOT DETECTED	TV DETECTED
HIV-1[f]	2×10^5	TV NOT DETECTED	TV DETECTED
Human papilloma virus 16[f]	6×10^5	TV NOT DETECTED	TV DETECTED
Kingella dentrificans	3×10^6	TV NOT DETECTED	TV DETECTED
Kingella kingae	1×10^7	TV NOT DETECTED	TV DETECTED
Klebsiella oxytoca	1×10^7	TV NOT DETECTED	TV DETECTED
Klebsiella pneumoniae	7×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus acidophilus	8×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus brevis	7×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus crispatus	2×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus jensonii	8×10^6	TV NOT DETECTED	TV DETECTED

Table 9. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Urine Matrix (Continued)

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Lactobacillus lactis	7×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus vaginalis	6×10^6	TV NOT DETECTED	TV DETECTED
Legionella pneumophila	5×10^6	TV NOT DETECTED	TV DETECTED
Leuconostoc paramensenteroides	7×10^6	TV NOT DETECTED	TV DETECTED
Listeria monocytogenes	1×10^7	TV NOT DETECTED	TV DETECTED
Micrococcus luteus	3×10^6	TV NOT DETECTED	TV DETECTED
Mobiluncus curtisii[b]	3×10^6	TV NOT DETECTED	TV DETECTED
Moraxella lacunata	6×10^6	TV NOT DETECTED	TV DETECTED
Moraxella osloensis	5×10^6	TV NOT DETECTED	TV DETECTED
Morganella morganii	1×10^7	TV NOT DETECTED	TV DETECTED
Mycobacterium smegmatis	7×10^6	TV NOT DETECTED	TV DETECTED
Mycoplasma genitalium	1×10^{6d}	TV NOT DETECTED	TV DETECTED
Mycoplasma hominis	1×10^{6d}	TV NOT DETECTED	TV DETECTED
Neisseria cinerea	1×10^6	TV NOT DETECTED	TV DETECTED
Neisseria dentrificans	2×10^6	TV NOT DETECTED	TV DETECTED
Neisseria elongata	7×10^6	TV NOT DETECTED	TV DETECTED
Neisseria flava	9×10^6	TV NOT DETECTED	TV DETECTED
Neisseria flavescens	8×10^6	TV NOT DETECTED	TV DETECTED
Neisseria gonorrhoeae	6×10^6	TV NOT DETECTED	TV DETECTED
Neisseria lactamica	3×10^6	TV NOT DETECTED	TV DETECTED
Neisseria mucosa	9×10^6	TV NOT DETECTED	TV DETECTED
Neisseria perflava	3×10^6	TV NOT DETECTED	TV DETECTED
Neisseria polysaccharea	4×10^6	TV NOT DETECTED	TV DETECTED
Neisseria sicca	8×10^6	TV NOT DETECTED	TV DETECTED
Neisseria subflava	9×10^6	TV NOT DETECTED	TV DETECTED
Pantoea agglomerans	4×10^6	TV NOT DETECTED	TV DETECTED
Paracoccus denitrificans	8×10^6	TV NOT DETECTED	TV DETECTED
Pentatrichomonis hominis[c]	1×10^6	TV NOT DETECTED	TV DETECTED
Peptostreptococcus anaerobius[b]	4×10^6	TV NOT DETECTED	TV DETECTED
Peptostreptococcus productus[b]	2×10^6	TV NOT DETECTED	TV DETECTED
Plesiomonas shigelloides	4×10^6	TV NOT DETECTED	TV DETECTED
Prevotella bivia[b]	1×10^6	TV NOT DETECTED	TV DETECTED
Propionibacterium acnes[b]	3×10^6	TV NOT DETECTED	TV DETECTED
Proteus mirabilis	1×10^7	TV NOT DETECTED	TV DETECTED
Proteus vulgaris	1×10^7	TV NOT DETECTED	TV DETECTED
Providencia stuartii	1×10^7	TV NOT DETECTED	TV DETECTED
Pseudomonas aeruginosa	8×10^6	TV NOT DETECTED	TV DETECTED

Table 9. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Urine Matrix (Continued)

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Pseudomonas fluorescens	8×10^6	TV NOT DETECTED	TV DETECTED
Pseudomonas putida	7×10^6	TV NOT DETECTED	TV DETECTED
Rahnella aquatilis	1×10^7	TV NOT DETECTED	TV DETECTED
Rhodospirillum rubrum	1×10^{6d}	TV NOT DETECTED	TV DETECTED
Saccharomyces cerevisiae[e]	6×10^6	TV NOT DETECTED	TV DETECTED
Salmonella minnesota	1×10^6	TV NOT DETECTED	TV DETECTED
Salmonella typhimurium	1×10^7	TV NOT DETECTED	TV DETECTED
Serratia marcescens	2×10^6	TV NOT DETECTED	TV DETECTED
Staphylococcus aureus	9×10^6	TV NOT DETECTED	TV DETECTED
Staphylococcus epidermidis	7×10^6	TV NOT DETECTED	TV DETECTED
Staphylococcus saprophyticus	8×10^6	TV NOT DETECTED	TV DETECTED
Streptococcus agalactiae	1×10^7	TV NOT DETECTED	TV DETECTED
Streptococcus bovis	8×10^6	TV NOT DETECTED	TV DETECTED
Streptococcus mitis	2×10^6	TV NOT DETECTED	TV DETECTED
Streptococcus mutans	2×10^7	TV NOT DETECTED	TV DETECTED
Streptococcus pneumoniae	1×10^6	TV NOT DETECTED	TV DETECTED
Streptococcus pyogenes	2×10^6	TV NOT DETECTED	TV DETECTED
Streptococcus salivarius	9×10^6	TV NOT DETECTED	TV DETECTED
Streptococcus sanguis	5×10^6	TV NOT DETECTED	TV DETECTED
Streptomyces griseinus	6×10^6	TV NOT DETECTED	TV DETECTED
Trichomonas tenax[c]	1×10^5	TV DETECTED	TV DETECTED
Trichomonas tenax[c]	1×10^3	TV DETECTED	TV DETECTED
Trichomonas tenax[c]	1×10^2	TV NOT DETECTED	TV DETECTED
Ureaplasma parvum	1×10^{6d}	TV NOT DETECTED	TV DETECTED
Ureaplasma urealyticum	1×10^6	TV NOT DETECTED	TV DETECTED
Vibrio parahaemolyticus	9×10^6	TV NOT DETECTED	TV DETECTED
Yersinia enterocolitica	8×10^6	TV NOT DETECTED	TV DETECTED

a. Tests run $\geq 10^6$ CFU/mL for bacteria and fungi, $\geq 10^6$ genomes/mL for yeast, $\geq 10^5$ $TCID_{50}$/mL or $\geq 10^5$ genomes/mL for viruses and $\geq 10^5$ cells/mL for protozoans.
b. Anaerobic organism
c. Protozoan
d. Genome equivalents tested (DNA)
e. Fungal organism
f. Virus

Table 10. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Vaginal Swab Matrix

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Achromobacter xerosis	1 x 10^6	TV NOT DETECTED	TV DETECTED
Acinetobacter calcoaceticus	3 x 10^6	TV NOT DETECTED	TV DETECTED
Acinetobacter lwoffii	6 x 10^6	TV NOT DETECTED	TV DETECTED
Actinomyces israelii[b]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Actinomyces pyogenes	8 x 10^6	TV NOT DETECTED	TV DETECTED
Aerococcus viridans	5 x 10^6	TV NOT DETECTED	TV DETECTED
Aeromonas hydrophila	5 x 10^6	TV NOT DETECTED	TV DETECTED
Alcaligenes faecalis	5 x 10^6	TV NOT DETECTED	TV DETECTED
Atopobium vaginae[b]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Bacillus subtilis	6 x 10^6	TV NOT DETECTED	TV DETECTED
Bacteroides fragilis[b]	5 x 10^6	TV NOT DETECTED	TV DETECTED
Bacteroides ureolyticus[b]	1 x 10^6	TV NOT DETECTED	TV DETECTED
Bifidobacterium adolescentis[b]	6 x 10^6	TV NOT DETECTED	TV DETECTED
Bifidobacterium brevi (breve)[b]	9 x 10^6	TV NOT DETECTED	TV DETECTED
Blastocystis hominis[c]	1 x 10^5 [d]	TV NOT DETECTED	TV DETECTED
Branhamella catarrhalis	3 x 10^6	TV NOT DETECTED	TV DETECTED
Brevibacterium linens	8 x 10^6	TV NOT DETECTED	TV DETECTED
Campylobacter jejuni	2 x 10^6	TV NOT DETECTED	TV DETECTED
Candida albicans[e]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Candida glabrata[e]	4 x 10^6	TV NOT DETECTED	TV DETECTED
Candida parapsilosi[e]	3 x 10^6	TV NOT DETECTED	TV DETECTED
Candida tropicalis[e]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Chlamydia trachomatis	2 x 10^6	TV NOT DETECTED	TV DETECTED
Chromobacterium violaceum	7 x 10^6	TV NOT DETECTED	TV DETECTED
Citrobacter freundii	1 x 10^6	TV NOT DETECTED	TV DETECTED
Clostridium difficile[b]	4 x 10^6	TV NOT DETECTED	TV DETECTED
Clostridium perfringens[b]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Corynebacterium genitalium	2 x 10^6	TV NOT DETECTED	TV DETECTED
Corynebacterium xerosis	3 x 10^6	TV NOT DETECTED	TV DETECTED
Cryptococcus neoformans[e]	5 x 10^6	TV NOT DETECTED	TV DETECTED
Cryptosporidium parvum[c]	1 x 10^5 [d]	TV NOT DETECTED	TV DETECTED
Cytomegalovirus[f]	5 x 10^5	TV NOT DETECTED	TV DETECTED

Table 10. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Vaginal Swab Matrix (Continued)

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Deinococcus radiodurans	1×10^6	TV NOT DETECTED	TV DETECTED
Derxia gummosa	1×10^{6} [d]	TV NOT DETECTED	TV DETECTED
Eikenella corrodens	8×10^6	TV NOT DETECTED	TV DETECTED
Entamoeba histolytica[c]	1×10^{5}[d]	TV NOT DETECTED	TV DETECTED
Enterobacter aerogenes	1×10^6	TV NOT DETECTED	TV DETECTED
Enterobacter cloacae	2×10^6	TV NOT DETECTED	TV DETECTED
Enterococcus avium	7×10^6	TV NOT DETECTED	TV DETECTED
Enterococcus faecalis	7×10^6	TV NOT DETECTED	TV DETECTED
Enterococcus faecium	3×10^6	TV NOT DETECTED	TV DETECTED
Erysipelothrix rhusiopathiae	3×10^6	TV NOT DETECTED	TV DETECTED
Escherichia coli	2×10^6	TV NOT DETECTED	TV DETECTED
Flavobacterium meningosepticum	5×10^6	TV NOT DETECTED	TV DETECTED
Fusobacterium nucleatum[b]	4×10^6	TV NOT DETECTED	TV DETECTED
Gardnerella vaginalis	2×10^6	TV NOT DETECTED	TV DETECTED
Gemella haemolysans	9×10^6	TV NOT DETECTED	TV DETECTED
Giardia intestinalis[c]	1×10^{5}[d]	TV NOT DETECTED	TV DETECTED
Haemophilus ducreyi	1×10^{6}[d]	TV NOT DETECTED	TV DETECTED
Haemophilus influenzae	3×10^6	TV NOT DETECTED	TV DETECTED
Herpes simplex virus I[f]	1×10^5	TV NOT DETECTED	TV DETECTED
Herpes simplex virus II[f]	1×10^5	TV NOT DETECTED	TV DETECTED
HIV-1[f]	2×10^5	TV NOT DETECTED	TV DETECTED
Human papilloma virus 16[f]	6×10^5	TV NOT DETECTED	TV DETECTED
Kingella dentrificans	3×10^6	TV NOT DETECTED	TV DETECTED
Kingella kingae	7×10^6	TV NOT DETECTED	TV DETECTED
Klebsiella oxytoca	1×10^6	TV NOT DETECTED	TV DETECTED
Klebsiella pneumoniae	7×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus acidophilus	9×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus brevis	7×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus crispatus	2×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus jensonii	9×10^6	TV NOT DETECTED	TV DETECTED
Lactobacillus lactis	1×10^7	TV NOT DETECTED	TV DETECTED
Lactobacillus vaginalis	2×10^6	TV NOT DETECTED	TV DETECTED
Legionella pneumophila	2×10^6	TV NOT DETECTED	TV DETECTED

Table 10. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Vaginal Swab Matrix (Continued)

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Leuconostoc paramensenteroides	9 x 10^6	TV NOT DETECTED	TV DETECTED
Listeria monocytogenes	8 x 10^6	TV NOT DETECTED	TV DETECTED
Micrococcus luteus	3 x 10^6	TV NOT DETECTED	TV DETECTED
Mobiluncus curtisii[b]	3 x 10^6	TV NOT DETECTED	TV DETECTED
Moraxella lacunata	1 x 10^6	TV NOT DETECTED	TV DETECTED
Moraxella osloensis	1 x 10^6	TV NOT DETECTED	TV DETECTED
Morganella morganii	2 x 10^6	TV NOT DETECTED	TV DETECTED
Mycobacterium smegmatis	1 x 10^6	TV NOT DETECTED	TV DETECTED
Mycoplasma genitalium	1 x 10^{6d}	TV NOT DETECTED	TV DETECTED
Mycoplasma hominis	1 x 10^{6d}	TV NOT DETECTED	TV DETECTED
Neisseria cinerea	1 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria dentrificans	7 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria elongata	8 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria flava	9 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria flavescens	8 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria gonorrhoeae	6 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria lactamica	1 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria mucosa	9 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria perflava	1 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria polysaccharea	4 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria sicca	1 x 10^6	TV NOT DETECTED	TV DETECTED
Neisseria subflava	9 x 10^6	TV NOT DETECTED	TV DETECTED
Pantoea agglomerans	4 x 10^6	TV NOT DETECTED	TV DETECTED
Paracoccus denitrificans	6 x 10^6	TV NOT DETECTED	TV DETECTED
Pentatrichomonis hominis[c]	1 x 10^6	TV NOT DETECTED	TV DETECTED
Peptostreptococcus anaerobius[b]	4 x 10^6	TV NOT DETECTED	TV DETECTED
Peptostreptococcus productus[b]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Plesiomonas shigelloides	4 x 10^6	TV NOT DETECTED	TV DETECTED
Prevotella bivia[b]	1 x 10^6	TV NOT DETECTED	TV DETECTED
Propionibacterium acnes[b]	3 x 10^6	TV NOT DETECTED	TV DETECTED
Proteus mirabilis	4 x 10^6	TV NOT DETECTED	TV DETECTED
Proteus vulgaris	7 x 10^6	TV NOT DETECTED	TV DETECTED
Providencia stuartii	2 x 10^6	TV NOT DETECTED	TV DETECTED

Table 10. Analytical Specificity/Competitive Interference Determination for Xpert TV Assay in Vaginal Swab Matrix (Continued)

Microorganism	Concentration Tested[a]	Xpert TV Assay Result	
		Cross-Reactivity (- *T. vaginalis*)	Competitive Interference (+ *T. vaginalis*)
Pseudomonas aeruginosa	4x 10^6	TV NOT DETECTED	TV DETECTED
Pseudomonas fluorescens	5 x 10^6	TV NOT DETECTED	TV DETECTED
Pseudomonas putida	4 x 10^6	TV NOT DETECTED	TV DETECTED
Rahnella aquatilis	2 x 10^6	TV NOT DETECTED	TV DETECTED
Rhodospirillum rubrum	1 x 10^{6d}	TV NOT DETECTED	TV DETECTED
Saccharomyces cerevisiae[e]	2 x 10^6	TV NOT DETECTED	TV DETECTED
Salmonella minnesota	1 x 10^6	TV NOT DETECTED	TV DETECTED
Salmonella typhimurium	5 x 10^6	TV NOT DETECTED	TV DETECTED
Serratia marcescens	2 x 10^6	TV NOT DETECTED	TV DETECTED
Staphylococcus aureus	9 x 10^6	TV NOT DETECTED	TV DETECTED
Staphylococcus epidermidis	5 x 10^6	TV NOT DETECTED	TV DETECTED
Staphylococcus saprophyticus	2 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus agalactiae	6 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus bovis	4 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus mitis	2 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus mutans	5 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus pneumoniae	1 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus pyogenes	2 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus salivarius	3 x 10^6	TV NOT DETECTED	TV DETECTED
Streptococcus sanguis	2 x 10^6	TV NOT DETECTED	TV DETECTED
Streptomyces griseinus	4 x 10^6	TV NOT DETECTED	TV DETECTED
Trichomonas tenax[c]	1 x 10^5	TV DETECTED	TV DETECTED
Trichomonas tenax[c]	1 x 10^3	TV DETECTED	TV DETECTED
Trichomonas tenax[c]	1 x 10^2	TV NOT DETECTED	TV DETECTED
Ureaplasma parvum	1 x 10^{6d}	TV NOT DETECTED	TV DETECTED
Ureaplasma urealyticum	1 x 10^6	TV NOT DETECTED	TV DETECTED
Vibrio parahaemolyticus	3 x 10^6	TV NOT DETECTED	TV DETECTED
Yersinia enterocolitica	3 x 10^6	TV NOT DETECTED	TV DETECTED

a. Tests run ≥ 10^6 CFU/mL for bacteria and fungi, ≥10^6 genomes/mL for yeast, ≥10^5 $TCID_{50}$/mL or ≥10^5 genomes/mL for viruses and ≥10^5 cells/mL for protozoans.
b. Anaerobic organism
c. Protozoan
d. Genome equivalents tested (DNA)
e. Fungal organism
f. Virus

Additional three microorganisms, *Dientamoeba fragilis, Agrobacterium radiobacter,* and *Erwinia herbicola,* were not available for direct testing. An *in silico* analysis was conducted using the Basic Local Alignment Search Tool (BLAST) to compare the Xpert TV Assay primer and probe sequences with all available sequences associated with these three microorganisms in the GenBank database. Available sequence data for *D. fragilis* was examined and showed a maximum of 7% homology to the Xpert TV primer and probe sequences. Available sequence data for *A. radiobacter* was examined and showed a maximum of 38% homology to the Xpert TV primer and probe sequences. Available sequence data for *E. herbicola* was examined and showed a maximum of 10% homology to the Xpert TV primer and probe sequences. Results are shown in Table 11.

Table 11. *In Silico* Analytical Specificity Determination for Xpert TV Assay

Strain	Accession Number	% Homology
Dientamoeba fragilis	KC967121.1	7%
Agrobacterium radiobacter	CP000629.1	38%
Erwinia herbicola	NG_035384.1	10%

17.4 Interfering Substances Study

The performance of the Xpert TV Assay was evaluated with potentially interfering endogenous and exogenous substances that may be present in the urogenital tract.

All substances were tested in the presence and absence of 3X LoD *T. vaginalis* (ATCC strain 30001) to determine if there was interference with the Xpert TV Assay. Substances were individually diluted into either pooled *Trichomonas vaginalis*-negative urine matrix (patient urine added to Cepheid Urine Transport Reagent) or pooled *Trichomonas vaginalis*-negative vaginal swab matrix (vaginal swabs collected into Cepheid Swab Transport Reagent). Positive and negative controls were included in the study.

For each interfering substance, eight replicates were tested for each set of samples (either *T. vaginalis* negative or *T. vaginalis* positive in clinical matrix). Tables 12 and 13 show the substances that were tested, the test concentrations, and the matrix in which they were diluted. One substance, blood at > 60% v/v demonstrated interference (result of **TV NOT DETECTED** in the presence of TV) in the vaginal swab matrix samples. Blood was subjected to repeat analysis at various lower concentrations until a result of **TV DETECTED** was obtained (50% v/v). For the other conditions and substances tested, all TV positive samples remained positive and all TV negative samples remained negative, indicating that there was no interference causing false negative or false positive results with the Xpert TV Assay for these substances.

Table 12. Potentially Interfering Substances in Urine Samples

Class/Substance	Active Ingredient	Concentration Tested
Blood	Blood	0.3% v/v, 1% v/v
Seminal Fluid	Seminal Fluid	5.0% v/v
Mucus	Mucin	0.8% w/v
Analgesics & Antibiotics	Acetylsalicylic Acid 500mg	40 mg/mL
	Acetaminophen	3.2 mg/mL
	Azithromycin	1.8 mg/mL
	Doxycycline	3.6 mg/mL
OTC Deodorant & Powders	PEG-20; PEG-32; PEG-20 Stearate	0.25% w/v
	Nanoxynol-9	0.25% w/v
Albumin	BSA	10 mg/mL
Glucose	Glucose	10 mg/mL
Bilirubin	Bilirubin	1 mg/mL
Acidic Urine (pH 4.0)	Urine + N-Acetyl-L-Cysteine	pH 4.0
Alkaline Urine (pH 9.0)	Urine + Ammonium Citrate	pH 9.0
Leukocytes	Leukocytes	10^5 cells/mL
Intravaginal Hormones	Progesterone; Estradiol	7 mg/mL Progesterone + 0.07 mg/mL Beta Estradiol

Table 13. Potentially Interfering Substances in Swab Samples

Class/Substance	Active Ingredient	Concentration Tested
Blood[a]	Blood	10%, 50%, 60% v/v
Seminal Fluid	Seminal Fluid	5.0% v/v
Mucus	Mucin	0.8% w/v
Over the counter (OTC) Vaginal Products; Contraceptives; Vaginal treatments	Benzocaine 5%; Resorcinol 2%	0.25% w/v
	Clotrimazole 2%	0.25% w/v
	Miconazole Nitrate 2%	0.25% w/v
	Tioconazole	0.25% w/v
	5% w/w Aciclovir	0.25% w/v
	Glycerin, Propylene glycol	0.25% w/v
	Glycerin; Carbomer	0.12% w/v
	Glycerin, Hydroxyethyl cellulose	0.25% w/v
	Goldenseal 3X HPUS; Kreosotum 12X HPUS	0.25% w/v
	Povidone-iodine 10%	0.25% v/v
	Nonoxynol-9 12.5%	0.25% w/v

Table 13. Potentially Interfering Substances in Swab Samples (Continued)

Class/Substance	Active Ingredient	Concentration Tested
Hemorrhoidal Cream	Glycerin 14%; Pramoxine HCl 1%	0.25% w/v
Leukocytes	Leukocytes	10^5 cells/mL
Intravaginal Hormones	Progesterone; Estradiol	7 mg/mL Progesterone + 0.07 mg/mL Beta Estradiol

a. In tests with substances diluted into pooled T. vaginalis-positive swab matrix, assay interference was observed in tests with blood at 60% v/v. No assay interference was observed in tests with blood at 50% v/v. This is addressed in Section 14, Limitations.

17.5 Carry-Over Contamination Study

This study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination in negative samples run after very high positive samples in the same GeneXpert module. A negative sample (*T. vaginalis* negative vaginal swabs in Cepheid Xpert Swab Transport Reagent) was run followed by 20 rounds of high positive sample (*T. vaginalis* ATCC 30001 at 10^6 cells/mL diluted in vaginal swab matrix) alternating with a negative sample in two separate GeneXpert modules for a total of 40 high positive and 42 negative samples for each module. This testing scheme resulted in a total of 82 runs (40 positive + 42 negative samples). There was no evidence of carry-over contamination as all 40 positive samples were correctly reported as **TV DETECTED** and all 42 negative samples were correctly reported as **TV NOT DETECTED**.

18 Reproducibility

Intra-site reproducibility of the Xpert TV Assay was evaluated at three sites (two external, one in-house). Site 1 used an Infinity-80 instrument. Sites 2 and 3 used GeneXpert Dx instruments. Specimens were created by spiking *Trichomonas vaginalis* (ATCC® 30001™) into pooled, *Trichomonas vaginalis* negative urine (patient urine added to Cepheid Urine Transport Reagent) or vaginal swab matrix (vaginal swabs collected into Cepheid Swab Transport Reagent). The specimens were prepared at concentration levels representing high negative (below LoD), LoD (~1X LoD), moderate positive (~3X LoD), and negative (*Trichomonas vaginalis* negative clinical matrix). A panel of 8 specimens (4 in urine and 4 in vaginal swab matrix) was tested twice per day, on 12 different days, by two different operators, at each of three sites (8 specimens x 2 replicates x 12 days x 2 operators x 3 sites = 1,152 observations total). Three lots of Xpert TV Assay cartridges were used at each of the 3 testing sites, with each lot used for 4 days of testing. Positive and negative controls were included in the study. The Xpert TV Assay was performed according to the Xpert TV Assay procedure. The rate of agreement with expected results is shown by site in Table 14.

Table 14. Summary of Reproducibility Results

Sample[a]	Site 1 (Infinity-80)			Site 2 (GeneXpert Dx)			Site 3 (GeneXpert Dx)			Total Agreement by Sample
	Op 1	Op 2	Site	Op 1	Op 2	Site	Op 1	Op 2	Site	
FS-Neg	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
FS-Mod Pos (~3X LoD; ~6 cells/mL)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
FS-LoD (~1X LoD; ~2 cells/mL)	95.8% (23/24)	100% (24/24)	97.9% (47/48)	87.5% (21/24)	95.8% (23/24)	91.7% (44/48)	100% (24/24)	95.8% (23/24)	97.9% (47/48)	95.8% (138/144)
FS-High Neg (below LoD <2 cells/mL)	87.5% (21/24)	75.0% (18/24)	81.3% (39/48)	66.7% (16/24)	79.2% (19/24)	72.9% (35/48)	79.2% (19/24)	70.8% (17/24)	75.0% (36/48)	76.4% (110/144)
UR-Neg	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)
UR-Mod Pos (~3X LoD; ~9 cells/mL)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144)

Table 14. Summary of Reproducibility Results (Continued)

Sample[a]	Site 1 (Infinity-80)			Site 2 (GeneXpert Dx)			Site 3 (GeneXpert Dx)			Total Agreement by Sample
	Op 1	Op 2	Site	Op 1	Op 2	Site	Op 1	Op 2	Site	
UR-LoD (~1X LoD; ~3 cells/mL)	75.0% (18/24)	91.7% (22/24)	83.3% (40/48)	83.3% (20/24)	91.3% (21/23)[b]	87.2% (41/47)	91.7% (22/24)	100% (24/24)	95.8% (46/48)	88.8% (127/143)
UR-High Neg (below LoD; < 3 cells/mL)	75.0% (18/24)	75.0% (18/24)	75.0% (36/48)	70.8% (17/24)	54.2% (13/24)	62.5% (30/48)	75.0% (18/24)	75.0% (18/24)	75.0% (36/48)	70.8% (102/144)

a. FS=female swab matrix; UR=urine matrix.
b. One sample indeterminate on initial and retest.

The reproducibility of the Xpert TV Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-lots, between-days, between-operators, and residual variability for each panel member are presented in Table 15.

Table 15. Summary of Reproducibility Data

Sample[a]	Assay Channel (Analyte)	N[b]	Mean Ct	Between-Site		Between-Lot		Between-Day		Between-Operator		Residual		Total	
				SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]
FS-Neg	SPC	144	33.7	0.0	0.0	0.1	23.2	0.1	8.9	0.0	0.0	0.4	67.9	0.4	1.2
FS-Mod Pos (~3X LoD; ~6 cells/mL)	TV	144	35.4	0.1	7.9	0.0	0.0	0.0	0.0	0.1	12.5	0.8	79.7	0.8	2.3
FS-LoD (~1X LoD; ~ 2 cells/mL)	TV	138	38.5	0.0	0.0	0.0	0.0	0.5	28.0	0.0	0.0	1.2	72.0	1.3	3.5
FS-High Neg (below LoD; < 2 cells/mL)	TV	110	39.4	0.0	0.0	0.0	0.0	0.4	17.6	0.0	0.0	1.7	82.4	1.8	4.5
UR-Neg	SPC	144	33.9	0.1	8.6	0.0	0.0	0.1	9.0	0.1	18.5	0.4	63.9	0.4	1.2
UR-Mod Pos (~3X LoD; ~9 cells/mL)	TV	144	35.5	0.2	22.3	0.1	9.6	0.0	0.0	0.0	0.0	0.6	67.9	0.7	1.9
UR-LoD (~1X LoD; ~3 cells/mL)	TV	127	39.3	0.0	0.0	0.4	24.4	0.0	0.0	0.0	0.0	1.2	75.6	1.3	3.4
UR-High Neg (below LoD; < 3 cells/mL)	TV	102	39.0	0.0	0.0	0.3	14.4	0.7	29.5	0.3	11.6	1.0	44.6	1.3	3.3

a. FS=female swab matrix; UR=urine matrix
b. Results with non-zero Ct values out of 144.
c. (%) is contribution of variance component to overall CV.

19 Instrument System Precision

An in-house precision study was conducted to compare the performance of the GeneXpert Dx and the GeneXpert Infinity Instrument Systems using specimens comprised of *Trichomonas vaginalis* (ATCC® 30001™) spiked into negative urine (patient urine added to Cepheid Urine Transport Reagent) or vaginal swab matrix (vaginal swabs collected into Cepheid Swab Transport Reagent). The specimens were prepared at concentration levels representing high negative (below LoD), LoD (~1X LoD), moderate positive (~3X LoD), and negative (*Trichomonas vaginalis* negative clinical matrix). A panel of 8 specimens (4 in urine matrix and 4 in vaginal swab matrix) was tested on 12 different days by two operators. Each operator conducted four runs of each panel specimen per day on each of the three instrument systems (8 specimens x 4 times/day x 12 days x 2 operators x 3 instrument systems = 2,304 observations total). Three lots of Xpert TV Assay cartridges were used for the study, with each lot used for 4 days of testing. Positive and negative controls were included in the study. The Xpert TV Assay was performed according to the Xpert TV Assay procedure. The rate of agreement with expected results is shown by instrument in Table 16.

Table 16. Summary of Precision Results

Sample[a]	GeneXpert Dx			Infinity-48			Infinity-80			% Total Agreement by Sample
	Op 1	Op 2	Inst	Op 1	Op 2	Inst	Op 1	Op 2	Inst	
FS-Neg	100% (48/48)	100% (48/48)	100% (96/96)	97.9% (47/48)	100% (48/48)	99.0% (95/96)	100% (48/48)	100% (48/48)	100% (96/96)	99.7% (287/288)
FS-Mod Pos (~3X LoD; ~6 cells/mL)	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100% (48/48)	100% (96/96)	100% (288/288)
FS-LoD (~1X LoD; ~ 2 cells/mL)	93.8% (45/48)	87.5% (42/48)	90.6% (87/96)	93.8% (45/48)	89.6% (43/48)	91.7% (88/96)	95.8% (46/48)	89.6% (43/48)	92.7% (89/96)	91.7% (264/288)
FS-High Neg (below LoD; < 2 cells/mL)	74.5% (35/47)	75.0% (36/48)	74.7% (71/95)	77.1% (37/48)	75.0% (36/48)	76.0% (73/96)	83.3% (40/48)	68.8% (33/48)	76.0% (73/96)	75.6% (217/287)[b]
UR-Neg	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100% (47/47)	100% (95/95)	100% (287/287)[b]
UR-Mod Pos (~3X LoD; ~9 cells/mL)	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100% (48/48)	100% (96/96)	100% (288/288)
UR-LoD (~1X LoD; ~3 cells/mL)	93.8% (45/48)	93.8% (45/48)	93.8% (90/96)	95.8% (46/48)	89.6% (43/48)	92.7% (89/96)	95.8% (46/48)	95.8% (46/48)	95.8% (92/96)	94.1% (271/288)
UR-High Neg (below LoD; < 3 cells/mL)	72.9% (35/48)	77.1% (37/48)	75.0% (72/96)	70.8% (34/48)	79.2% (38/48)	75.0% (72/96)	81.3% (39/48)	85.4% (41/48)	83.3% (80/96)	77.8% (224/288)

a. FS=female swab matrix; UR=urine matrix.
b. One FS-Low Pos and one UR-Neg sample indeterminate and not retested.

The precision of the Xpert TV Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-instruments, between-lots, between-days, between-operators, and residual variability for each panel member are presented in Table 17.

Table 17. Summary of Precision Data

Sample[a]	Assay Channel (Analyte)	N[b]	Mean Ct	Between-Instrument		Between-Lot		Between-Day		Between-Operator		Residual		Total	
				SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]	SD	CV (%)[c]
FS-Neg	SPC	288	31.9	0.0	0.0	0.3	53.5	0.0	0.0	0.1	1.9	0.2	44.6	0.4	1.1
FS-Mod Pos (~3X LoD; ~6 cells/mL)	TV	288	35.2	0.0	0.0	0.3	22.4	0.0	0.0	0.1	4.5	0.4	73.1	0.5	1.5
FS-LoD (~1X LoD; ~2 cells/mL)	TV	264	39.0	0.2	3.3	0.1	0.4	0.2	1.3	0.0	0.0	1.3	95.0	1.3	3.4
FS-High Neg (below LoD; < 2 cells/mL)	TV	217	39.4	0.0	0.0	0.0	0.0	0.0	0.0	0.2	1.6	1.3	98.4	1.3	3.2
UR-Neg	SPC	287	32.4	0.0	0.0	0.3	47.2	0.1	2.9	0.0	0.0	0.3	49.9	0.4	1.2
UR-Mod Pos (~3X LoD; ~9 cells/mL)	TV	288	35.4	0.0	0.0	0.4	30.4	0.0	0.0	0.2	11.3	0.5	58.3	0.6	1.8
UR-LoD (~1X LoD; ~3 cells/mL)	TV	271	38.2	0.0	0.0	0.5	13.6	0.6	16.2	0.3	3.6	1.2	66.5	1.4	3.7
UR-High Neg (below LoD; < 3 cells/mL)	TV	224	38.9	0.0	0.0	0.3	5.4	0.0	0.0	0.3	4.2	1.2	90.3	1.3	3.3

a. FS=female swab matrix; UR=urine matrix
b. Results with non-zero Ct values out of 288.
c. (%) is contribution of variance component to overall CV.

20 References

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8. 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

Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089
United States

Telephone: + 1 408 541 4191

Fax: + 1 408 541 4192

www.cepheid.com

European Headquarters

Cepheid Europe SAS
Vira Solelh
81470 Maurens-Scopont
France

Telephone: + 33 563 825 300

Fax: + 33 563 825 301

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

Contact Information

United States	France
Telephone: + 1 888 838 3222	Telephone: + 33 563 825 319
Email: techsupport@cepheid.com	Email: support@cepheideurope.com

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

23 Table of Symbols

Symbol	Meaning
REF	Catalog number
IVD	*In vitro* diagnostic medical device
CE	CE marking – European Conformity
EC REP	Authorized Representative in the European Community
CH REP	Authorized Representative in Switzerland
	Importer
	Do not reuse
LOT	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <n> tests
CONTROL	Control
	Expiration date
	Temperature limitation
	Biological risks
	Warning

Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089
USA
Phone: + 1 408 541 4191
Fax: + 1 408 541 4192
www.cepheid.com

Cepheid Europe SAS
Vira Solelh
81470 Maurens-Scopont
France
Phone: + 33 563 825 300
Fax: + 33 563 825 301

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

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