GeneXpert®
Powered By CEPHEID INNOVATION

Xpert® CT

REF **GXCT-CE-10**

Cepheid®

***In Vitro* Diagnostic Medical Device**

CE 2797 IVD

301-0819, Rev. J March 2023

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CE 2797 IVD

Xpert® CT

For *In Vitro* Diagnostic Use only.

1 Proprietary Name

Xpert® CT

2 Common or Usual Name

Xpert CT Assay

3 Intended Use

The Xpert CT Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* real-time PCR test for the automated detection and differentiation of genomic DNA from *Chlamydia trachomatis* (CT) to aid in the diagnosis of chlamydial urogenital disease. The assay may be used to test the following specimens from asymptomatic and symptomatic individuals: female and male urine, endocervical swab, and patient-collected vaginal swab (collected in a clinical setting).

4 Summary and Explanation

Chlamydia trachomatis (CT) are Gram-negative, non-motile, bacteria that exist as obligate intracellular parasites of eukaryotic cells due to their inability to synthesize ATP. The CT species is comprised of at least fifteen serovars that can cause disease in humans; serovars D through K are the major cause of genital chlamydial infections in men and women[1]. Left untreated, CT can cause non-gonococcal urethritis, epididymitis, proctitis, cervicitis, and acute salpingitis. In women, untreated CT can lead to pelvic inflammatory disease (PID) in more than 40% of the infected population and render up to 20% infertile. PID can manifest as endometritis, salpingitis, pelvic peritonitis, and tubo-ovarian abscesses.[2,3,4,5,6]

5 Principle of the Procedure

The Xpert CT Assay is an automated *in vitro* diagnostic test for qualitative detection and differentiation of DNA from CT. The assay is performed on the Cepheid GeneXpert Instrument Systems.

The GeneXpert Instrument Systems automate and integrate sample purification, nucleic acid amplification, and detection of the target sequences in simple or complex samples using real-time PCR and RT-PCR assays. The systems consist of an instrument, personal computer, and preloaded software for running tests on collected samples and viewing the results. The systems require the use of single-use disposable cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between cartridges during the testing process is minimized. For a full description of the systems, refer to the appropriate GeneXpert Instrument System Operator Manual.

The Xpert CT Assay includes reagents for the 5' exonuclease real-time PCR detection of CT. Reagents for the detection of 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 bacteria 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 sample contains human DNA. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability. The primers and probes in the Xpert CT Assay detect chromosomal sequences in the bacteria. One target is detected for CT (CT1).

The Xpert CT Assay is designed for use with the following specimens collected from symptomatic and asymptomatic individuals: first-catch male urine, female urine, endocervical specimens and vaginal swab specimens. The urine transport reagent and swab transport reagent are included in the Xpert CT/NG Urine Specimen Collection Kit, Xpert Urine Specimen Collection Kit, the Xpert CT/NG Vaginal/Endocervical Specimen Collection Kit, Xpert Swab Specimen Collection Kit, and the Xpert Vaginal/Endocervical Collection Kit and are designed to preserve patient specimens to allow transport to the laboratory prior for analysis with Xpert CT Assay.

The specimen is briefly mixed by inverting the collection tube several times and/or aspirating with a transfer pipette. Using the supplied transfer pipette, the sample is pipetted above the fill mark on the transfer pipette and transferred to the sample chamber of the Xpert CT cartridge. The GeneXpert cartridge is loaded onto the GeneXpert Instrument System platform, which performs hands-off, automated sample processing, and real-time PCR for detection of DNA. Summary and detailed test results are obtained in approximately 90 minutes and are displayed in tabular and graphic formats.

6 Reagents and Instruments

6.1 Material Provided

The Xpert CT Assay kit (GXCT-CE-10) contains sufficient reagents to process 10 quality control samples and/or specimens.

The kit contains the following:

Xpert CT Cartridges with Integrated Reaction Tubes	**10 per kit**
• Bead 1, Bead 2, and Bead 3	1 of each per cartridge
• Elution Reagent	2.0 mL per cartridge
• Lysis Reagent (Guanidinium thiocyanate)	2.5 mL per cartridge
• Wash Reagent	0.5 mL per cartridge
• Binding Reagent	3.0 mL per cartridge
Transfer pipettes (1 mL)	**10 per kit**
CD	**1 per kit**
• Assay Definition Files (ADF)	
• Instructions to import ADF into software	
• Instructions for Use (Package Insert)	

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

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

7 Storage and Handling

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

8 Materials Required but Not Provided

- Primary samples must be collected and treated with the appropriate kit:
  - Xpert CT/NG Vaginal/Endocervical Specimen Collection kit (CT/NGSWAB-50) or Xpert Vaginal/Endocervical Specimen Collection Kit (SWAB/A-50) or Xpert Swab Specimen Collection Kit (SWAB/G-50)
  - Xpert CT/NG Urine Specimen Collection kit (CT/NGURINE-50) or Xpert Urine Specimen Collection Kit (URINE/A-50)
- 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

- Printer: If a printer is needed, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.

9 Materials Available but Not Provided

For information regarding commercial external controls for use with this assay, please contact your Cepheid representative or Cepheid Technical Support. External controls should be used in accordance with local regulatory requirements.

10 Warnings and Precautions

10.1 General

- For *in vitro* diagnostic use.
- Pathogenic microorganisms, including hepatitis viruses and Human Immunodeficiency Virus, may be present in clinical specimens. 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. Center for Disease Control and Prevention and the Clinical and Laboratory Standards Institute.[7,8]
- 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.

10.2 Specimen

- For collection of endocervical swab specimens and patient-collected vaginal swab specimens, use only the Xpert CT/NG Vaginal/Endocervical Specimen Collection Kit (CT/NGSWAB-50) or Xpert Vaginal/Endocervical Specimen Collection Kit (SWAB/A-50) or Xpert Swab Specimen Collection Kit (SWAB/G-50).
- For urine specimens, use only the Xpert CT/NG Urine Specimen Collection Kit (CT/NGURINE-50) or Xpert Urine Specimen Collection Kit (URINE/A-50) or unpreserved (neat) urine.
- Under or over dispensing of urine into 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 Swab Transport Reagent tube.
- Urine specimens must be tested before the expiration date of the Urine Transport Reagent tube.
- 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.

10.3 Assay/Reagent

- Do not substitute Xpert CT Assay reagents with other reagents.
- Do not open the Xpert CT Assay cartridge lid except when adding the sample.
- Do not use a cartridge that has been dropped or shaken.
- Do not place the sample ID label on the cartridge lid or on the bar code label.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use Xpert CT Assay cartridge is used to process one test. Do not reuse processed cartridges.
- Use of NG positive controls in the CT only assay mode may lead to invalid control results.
- 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.
- 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.
- 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 of 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.

11 Chemical Hazards[9,10]

- Signal Word: WARNING
- **UN GHS Hazard Statements**
  - Harmful if swallowed
  - May be harmful in contact to skin
  - Causes eye irritation
- **UN GHS Precautionary Statements**
  - **Prevention**
    - Wash thoroughly after handling
  - **Response**
    - If skin irritation occurs: Get medical advice/attention.
    - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
    - If eye irritation persists: Get medical advice/attention.
    - Call a POISON CENTER or doctor/physician if you feel unwell.
  - **Storage/Disposal**
    - Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

12 Specimen Collection and Transport

Collect specimens only with a Cepheid collection kit:

12.1 Xpert CT/NG Urine Specimen Collection Kit (CT/NGURINE-50) or Xpert Urine Specimen Collection Kit (URINE/A-50)

First catch female urine specimen must be transferred to the Xpert CT/NG Urine Transport Reagent tube or Xpert Urine Transport Reagent tube within 24 hours of primary collection if shipped and/or stored at room temperature.

First catch male urine specimen must be transferred to the Xpert CT/NG Urine Transport Reagent tube or Xpert Urine Transport Reagent tube within 3 days of primary collection if shipped and/or stored at room temperature.

First catch male and female urine specimen NOT transferred to the Xpert CT/NG Urine Transport Reagent tube or Xpert Urine Transport Reagent tube (unpreserved urine specimen) can be shipped and/or stored for up to 8 days at 4 °C.

- First catch female urine specimen that is transferred to the Xpert CT/NG Urine Transport Reagent tube or Xpert Urine Transport Reagent tube (preserved female urine specimen) can be shipped and/or stored up to 45 days at 2 °C to 15 °C, or up to 3 days at 2 °C to 30 °C before testing with the Xpert CT Assay.
- First catch male urine specimen that is transferred to the Xpert CT/NG Urine Transport Reagent tube or Xpert Urine Transport Reagent tube (preserved male urine specimen) can be shipped and/or stored up to 45 days at 2 °C to 30 °C before testing with the Xpert CT Assay.

12.2 Xpert CT/NG Vaginal/Endocervical Specimen Collection Kit (CT/NGSWAB-50) or Xpert Vaginal/Endocervical Specimen Collection Kit (SWAB/A-50) or Xpert Swab Specimen Collection Kit (SWAB/G-50)

- Swab samples stored in Xpert CT/NG Swab Transport Reagent tubes or Xpert Swab Transport Reagent tubes should be transported to the laboratory at 2 °C to 30 °C.
- Swab samples in Xpert CT/NG Swab Transport Reagent tubes or Xpert Swab Transport Reagent tubes are stable up to 60 days at 2 °C to 30 °C before testing with the Xpert CT Assay.

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

13 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 version 6.1 or higher.

13.1 Preparing the Cartridge

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

To add the sample to the Xpert CT Assay cartridge:

1. Obtain the following items:
   - Xpert CT cartridge
   - Transfer pipette (provided)
   - Appropriately collected and labeled test sample
2. Open the cartridge lid.
3. Gently invert the transport tube 3 to 4 times to ensure adequate mixing of sample and transport matrix.
4. Unwrap the transfer pipette.
5. Open the transport tube lid, compress the bulb of the transfer pipette, insert the pipette into the transport tube, and release the bulb to fill the transfer pipette above the mark on the pipette shaft (Figure 1). Ensure the pipette is filled with no air bubbles present.

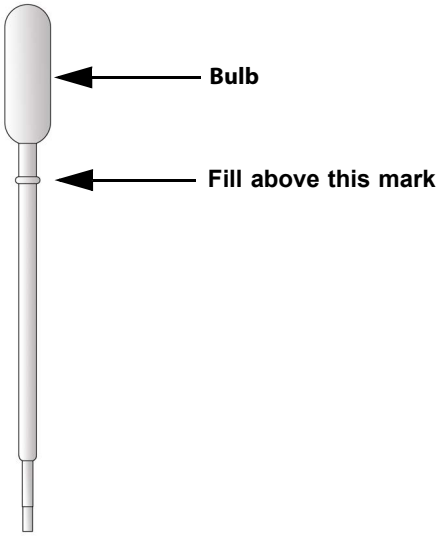

Figure 1. Transfer Pipette and Fill Mark

6. Empty the pipette's content into the Sample chamber of the cartridge (Figure 2).

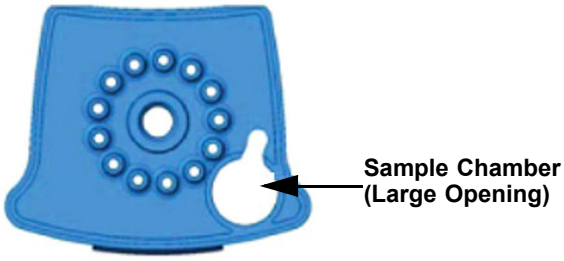

Figure 2. Xpert CT Assay Cartridge (Top View)

7. Close the cartridge lid.

13.2 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 CT 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 system:
   - 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 shortcut 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 shortcut icon on the Windows desktop.
2. Log on to the GeneXpert Instrument System software using your user name and password.
3. In the GeneXpert System window, click **Create Test** (GeneXpert Dx) or click **Orders** and **Order Test** (Infinity). The **Create Test** window 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 associated with the test results and is shown in the View Results window.
5. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is associated with the test results and is shown in the View Results window and all reports. The Scan Cartridge dialog box appears.
6. Scan the barcode on the Xpert CT Assay cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Reagent Lot ID, Cartridge SN, and Expiration Date.

Note If the barcode on the Xpert CT Assay cartridge does not scan, then repeat the test with a new cartridge following the procedure in Section 18, 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 and removing the cartridge.

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

14 Viewing and Printing Results

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

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

15 Quality Control

CONTROL

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

- **Sample Processing Control (SPC):** Ensures the sample was processed correctly. The SPC contains genomic DNA of *Bacillus globigii* that is included in each cartridge. The SPC verifies that binding and elution of target DNA have occurred if the organisms are present and verifies that 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):** Ensures 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 taken 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 assigned acceptance criteria.

15.1 External Controls:

External controls (one positive and one negative) may be used in accordance with local, state, and federal accrediting organizations as applicable.

16 Interpretation of Results

The results are interpolated by the GeneXpert Instrument System from measured fluorescent signals and embedded calculation algorithms and will be shown in the View Results window. The Xpert CT Assay provides test results for the CT target, according to the algorithms shown in Table 1.

Table 1. All Possible Final Test Results for CT Assay

RESULT TEXT	CT1	SPC	SAC
CT DETECTED	+	+/-	+/-
CT NOT DETECTED	-	+	+
INVALID	-	-	+/-
INVALID	-	+/-	-

Possible results are shown in Table 2.

Table 2. Xpert CT Assay Results and Interpretation

Result	Interpretation
CT DETECTED See Figure 3.	CT target DNA sequence is detected. • PCR amplification of the CT target gives Ct within the valid range and fluorescence endpoints above the minimum setting. • SPC: Not applicable. The SPC is ignored because CT target amplification can compete with this control. • SAC: Not applicable. The SAC is ignored because CT target amplification can compete with this control. • PCC: PASS; all probe check results pass.
CT NOT DETECTED See Figure 4.	CT target DNA sequence is not detected. • CT is absent or below the assay detection level. • SPC: PASS; PCR amplification of the SPC target gives a Ct within the valid range and a fluorescence endpoint above the minimum setting. • SAC: PASS; PCR amplification of the SAC target gives a Ct within the valid range and a fluorescence endpoint above the minimum setting. • PCC: PASS; all probe check results pass.

Table 2. Xpert CT Assay Results and Interpretation (Continued)

Result	Interpretation
INVALID See Figure 5.	Presence or absence of CT target DNA cannot be determined. Repeat test according to the instructions in Section 18, Retest Procedure. • SPC: FAIL; SPC target result is negative and the SPC Ct is not within valid range and endpoint below minimum setting. • SAC: PASS; SAC has a Ct within the valid range and fluorescence endpoint above the minimum setting. • PCC: PASS; all probe check results pass. Or • SPC: PASS; SPC has a Ct within the valid range and fluorescence endpoint above the minimum setting. • SAC: FAIL; SAC target result is negative. The SAC Ct is not within valid range and fluorescence endpoint is below the minimum setting. • PCC: PASS; all probe check results pass. Or • SPC: FAIL; SPC target result is negative, the SPC Ct is not within valid range and fluorescence endpoint is below the minimum setting. • SAC: FAIL; SAC target result is negative. The SAC Ct is not within valid range and fluorescence endpoint is below the minimum setting. • PCC: PASS; all probe check results pass.
ERROR	Presence or absence of CT target DNA cannot be determined. Repeat test according to the instructions in Section 18, Retest Procedure. • SPC: NO RESULT • SAC: NO RESULT • PCC: FAIL*; all or one of the probe check results fail. The PCC probably failed because the reaction tube was filled improperly or a probe integrity problem was detected. * If the probe check passed, the error is caused by a system component failure.
NO RESULT	Presence or absence of CT target DNA cannot be determined. Repeat test according to the instructions in Section 18, Retest Procedure. A **NO RESULT** indicates insufficient data were collected. For example, the operator stopped a test that was in progress. • SPC: NO RESULT • SAC: NO RESULT • PCC: NA (Not applicable)

Note The screens shown in this section (Figure 3, Figure 4, and Figure 5) are from a GeneXpert Dx instrument running GeneXpert Dx software.

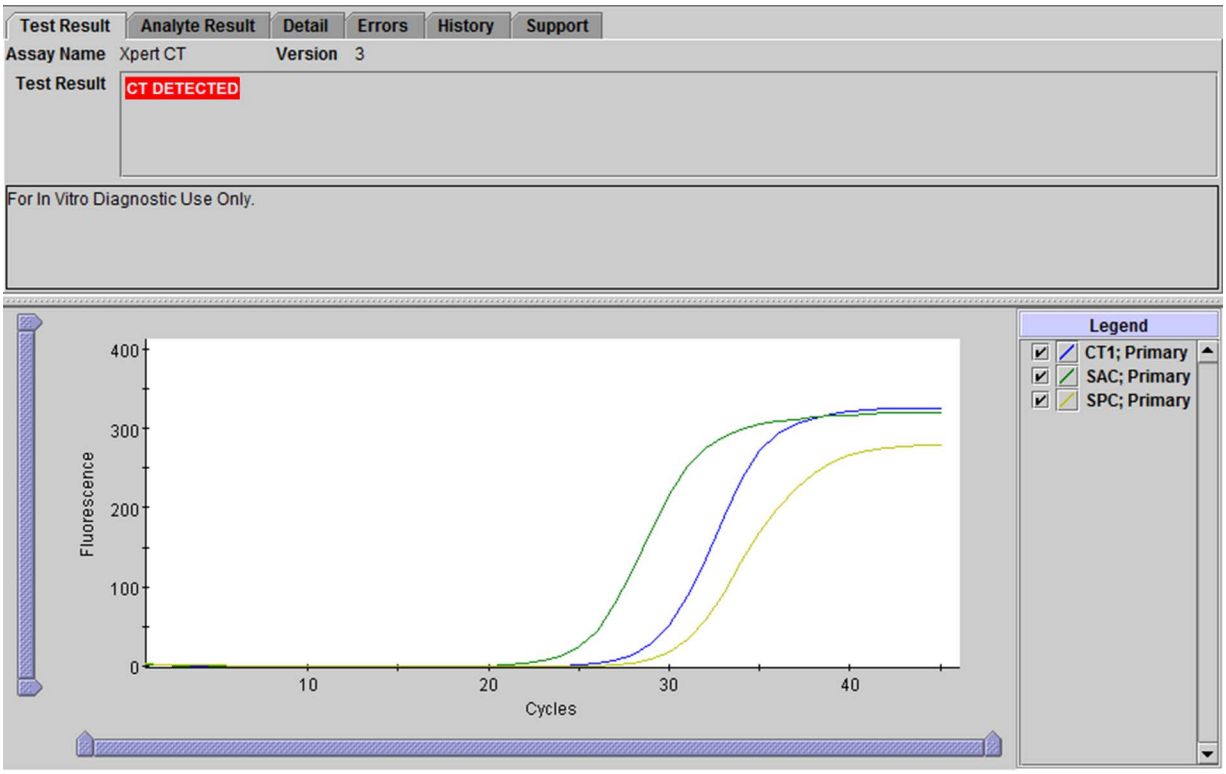

Figure 3. An Example of a CT DETECTED Result

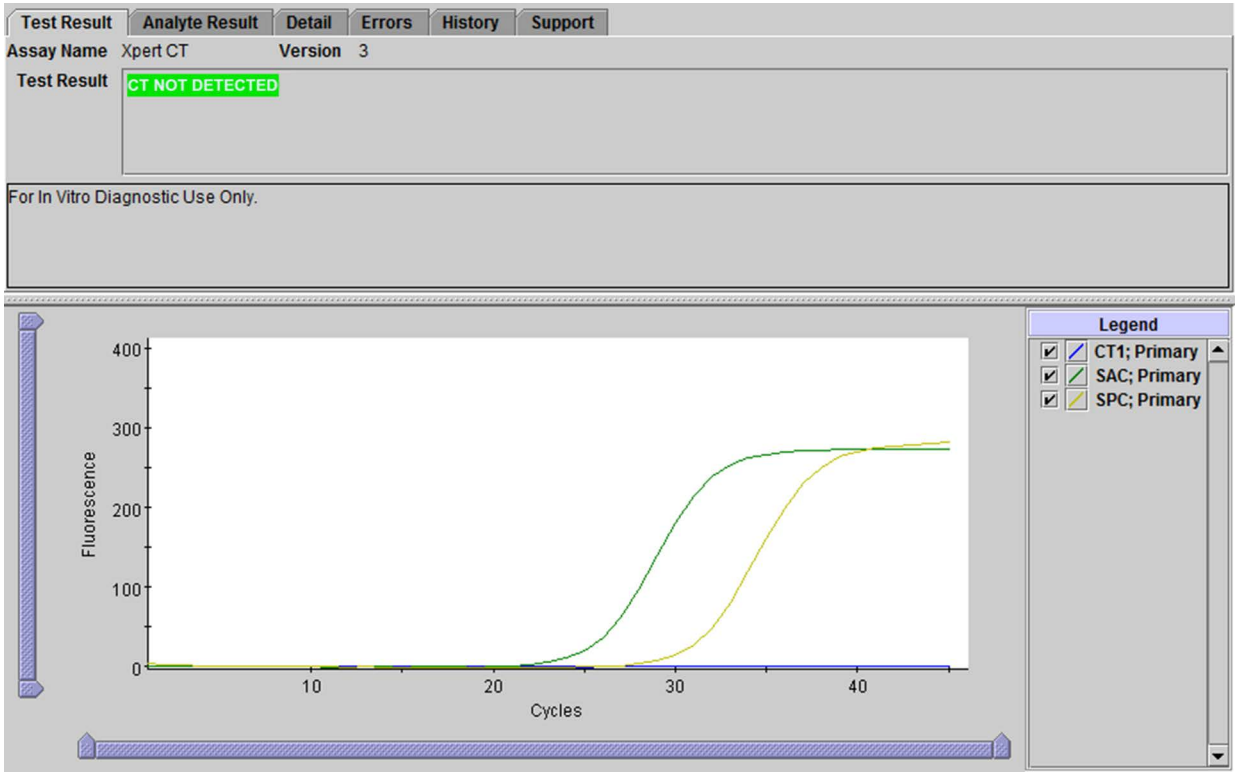

Figure 4. An Example of a CT NOT DETECTED Result

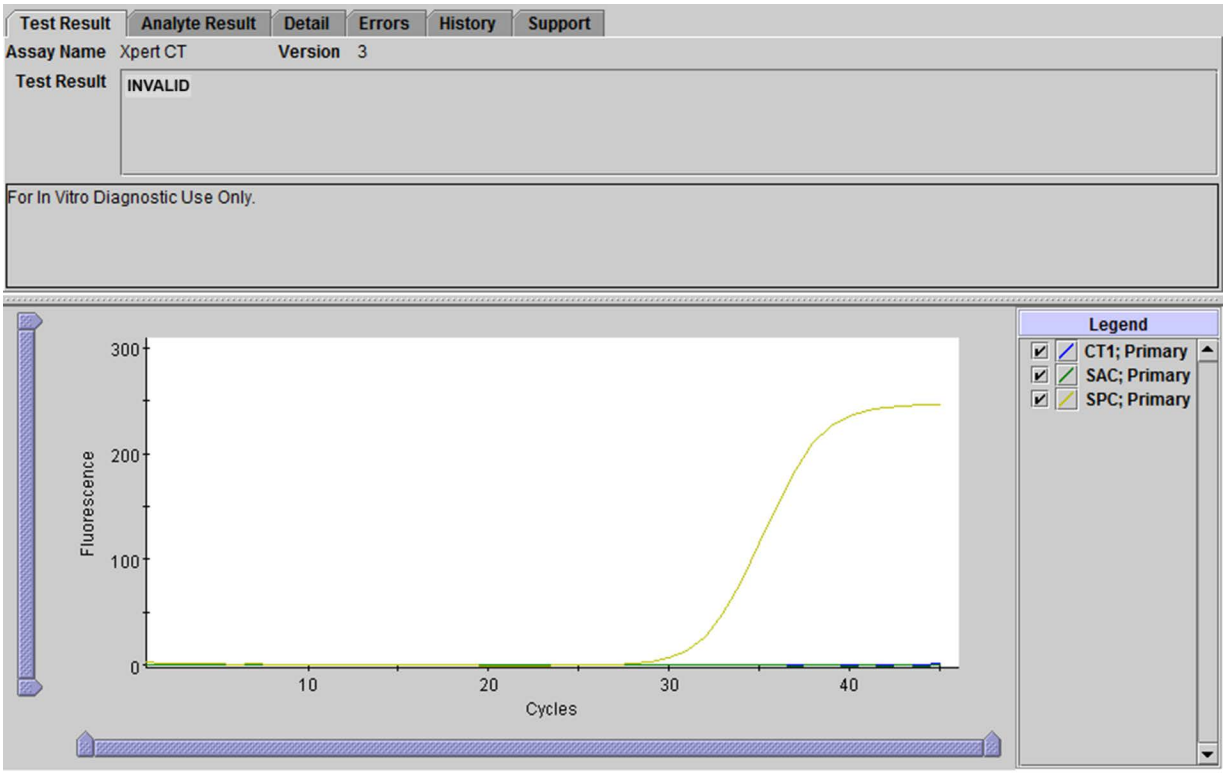

Figure 5. An Example of an INVALID Result

17 Reasons to Repeat the Assay

The specimen should be retested if any of the following results are obtained from the first test. Repeat the test according to the instructions in Section 18, Retest Procedure.

- 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 inadequate.
- An **ERROR** result indicates that the PCC failed and the assay was aborted 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.

18 Retest Procedure

Obtain the leftover treated sample from the CT/NG Swab Transport Reagent, Xpert Swab Transport Reagent, CT/NG Urine Transport Reagent or Urine Transport Reagent tube. Repeat the test with a new cartridge. If the leftover treated 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.

19 Limitations

- The Xpert CT Assay has only been validated with the following specimen types, collected with the Cepheid Xpert CT/NG Vaginal/Endocervical, Xpert Vaginal/Endocervical, Xpert CT/NG Urine, Xpert Swab Specimen Collection Kit, or Xpert Urine Specimen Collection Kits:
  - Endocervical swabs
  - Patient-collected vaginal swabs
  - Male and female urine
- Erroneous test results might occur from improper specimen collection, technical error, sample mix-up, or because the number of organisms are below the limit of detection of the test.
- Careful compliance with the instructions in this insert and to the Swab and Urine Collection Kit instruction documents are necessary to avoid erroneous results.
- The Xpert CT Assay has been validated using the procedures provided in this package insert only. Modification to these procedures may alter the performance of the test.
- Because the detection of CT is dependent on the DNA present in the sample, reliable results are dependent on proper sample collection, handling and storage.
- With endocervical and patient-collected vaginal specimens, assay interference may be observed in the presence of: blood (>1% v/v) or mucin (>0.8% w/v).
- With urine specimens, assay interference may be observed in the presence of: blood (>0.3% v/v), mucin (>0.2% w/v), bilirubin (>0.2 mg/mL), or Vagisil feminine powder (>0.2% w/v).
- Collection and testing of urine specimens with the Xpert CT Assay is not intended to replace cervical exam and endocervical sampling for diagnosis of urogenital infection. Other genitourinary tract infections can be caused by other infectious agents.
- The effects of other potential variables such as vaginal discharge, use of tampons, douching, and specimen collection variables have not been determined.
- A negative test result does not exclude the possibility of infection because test results may be affected by improper specimen collection, technical error, specimen mix-up, concurrent antibiotic therapy, or the number of organisms in the specimen which may be below the sensitivity of the test.
- The Xpert CT Assay should not be used for the evaluation of suspected sexual abuse or for other medico-legal indications. Additional testing is recommended in any circumstance when false positive or false negative results could lead to adverse medical, social, or psychological consequences.
- The Xpert CT 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 predictive value of an assay depends on the prevalence of the disease in any particular population. See Table 3 through Table 6 for hypothetical predictive values when testing varied populations.
- Xpert CT Assay performance has not been evaluated in patients less than 14 years of age.
- Xpert CT Assay performance has not been evaluated in patients with a history of hysterectomy.
- The patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated.
- The Xpert CT 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 CT Assay has not been evaluated with patients who are currently being treated with antimicrobial agents active against CT.
- As with many diagnostic tests, results from the Xpert CT Assay should be interpreted in conjunction with other laboratory and clinical data available to the physician.
- Mutations or other changes within the regions of the bacterial genomes covered by the primers and/or probes in the Xpert assay may result in failure to detect the target organisms.

20 Expected Values

The prevalence of infection with CT in patient populations depend 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 CT Assay, the observed CT prevalence rates in females and males were 5.4% and 5.7%, respectively.

20.1 Positive and Negative Predictive Values

Hypothetical estimated positive and negative predictive values (PPV and NPV) for different prevalence rates using the Xpert CT Assay are shown in Table 3 through Table 6 below. These calculations are based on a hypothetical prevalence and the overall sensitivity and specificity (compared to the patient infected status) observed during the Xpert CT multi-center clinical study (Table 7).

In patient-collected vaginal swab specimens, the overall sensitivity and specificity for CT were 99.5 and 99.1%, respectively (Table 7). Table 3 shows PPV and NPV for patient-collected vaginal swab specimens using hypothetical prevalence rates.

Table 3. Hypothetical PPV and NPV– Patient-collected Vaginal Swabs

Prevalence Rate (%)	CT			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	99.5	99.1	53.6	100
2	99.5	99.1	70.0	100
5	99.5	99.1	85.8	100
10	99.5	99.1	92.7	99.9
15	99.5	99.1	95.3	99.9
20	99.5	99.1	96.6	99.9
25	99.5	99.1	97.4	99.8
30	99.5	99.1	98.0	99.8
50	99.5	99.1	99.1	99.5

In endocervical swab specimens, the overall sensitivity and specificity for CT were 96.0% and 99.6%, respectively (Table 7). Table 4 shows PPV and NPV for endocervical swab specimens using hypothetical prevalence rates.

Table 4. Hypothetical PPV and NPV– Endocervical Swabs

Prevalence Rate (%)	CT			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	96.0	99.6	68.3	100
2	96.0	99.6	81.3	99.9
5	96.0	99.6	91.8	99.8
10	96.0	99.6	96.0	99.6
15	96.0	99.6	97.4	99.3
20	96.0	99.6	98.2	99.0
25	96.0	99.6	98.6	98.7
30	96.0	99.6	98.9	98.3
50	96.0	99.6	99.5	96.2

In female urine specimens, the overall sensitivity and specificity for CT were 98.1% and 99.8%, respectively (Table 7). Table 5 shows PPV and NPV for female urine specimens using hypothetical prevalence rates.

Table 5. Hypothetical PPV and NPV– Female Urine

Prevalence Rate (%)	CT			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	98.1	99.8	85.5	100
2	98.1	99.8	92.2	100
5	98.1	99.8	96.8	99.9
10	98.1	99.8	98.5	99.8
15	98.1	99.8	99.0	99.7
20	98.1	99.8	99.3	99.5
25	98.1	99.8	99.5	99.4
30	98.1	99.8	99.6	99.2
50	98.1	99.8	99.8	98.1

In male urine specimens, the overall sensitivity and specificity for CT were 98.5% and 99.8%, respectively (Table 7). Table 6 shows PPV and NPV for male urine specimens using hypothetical prevalence rates.

Table 6. Hypothetical PPV and NPV– Male Urine

Prevalence Rate (%)	CT			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	98.5	99.8	82.2	100
2	98.5	99.8	90.3	100
5	98.5	99.8	96.0	99.9
10	98.5	99.8	98.1	99.8
15	98.5	99.8	98.8	99.7
20	98.5	99.8	99.1	99.6
25	98.5	99.8	99.3	99.5
30	98.5	99.8	99.5	99.3
50	98.5	99.8	99.8	98.5

21 Performance Characteristics

21.1 Clinical Performance

Performance characteristics of the Xpert CT Assay were determined in a multi-site prospective investigational study at 36 US and UK institutions by comparing the Xpert CT Assay to a patient infected status (PIS) algorithm based on combined results from two currently marketed NAAT tests.

Study participants included consenting asymptomatic and symptomatic, sexually active males and females, including pregnant women, seen at locations including, but not limited to: OB/GYN, sexually transmitted disease (STD), teen, public health, and family planning clinics. The average age among female study participants was 30.3 years (range = 14 to 83 years); the average age among male study participants was 37.7 years (range = 17 to 74 years).

The study specimens consisted of prospectively collected male urine, female urine, endocervical swabs, urethral swabs and patient-collected vaginal swabs (collected in a clinical setting).

A female study participant was categorized as infected (I) by PIS for CT if at least one positive result was reported from each reference NAAT test. If both NAAT tests resulted in equivocal results for both sample types (swab and urine), the PIS status was defined as equivocal (EQ). This is the only scenario for an overall PIS of EQ; no study participants fell into this category for this study. Female study participants with positive results on both reference urine specimens and negative results on both reference swab specimens were categorized as infected (I) for urine and not infected (NI) for the swab specimen. Any other combination of results was categorized as not infected (NI).

A male study participant was categorized as infected (I) by PIS for CT if at least one positive result was reported from each reference NAAT test. If both NAAT tests resulted in equivocal results for both sample types (swab and urine), the PIS status was defined as equivocal (EQ). This is the only scenario for an overall PIS of EQ; no study participants fell into this category for this study. Any other combination of results was categorized as not infected (NI).

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

During the clinical evaluation of the Xpert CT Assay, a total of 212 female subjects were infected with CT. Symptoms were reported in 41.0% (87/212) of infected and 34.1% (1221/3579) non-infected female subjects. A total of 196 male subjects were infected with CT. Symptoms were reported in 62.8% (123/196) of infected and 18.0% (584/3248) non-infected male subjects.

Among the 14,790 tests performed, 416 had to be retested due to **ERROR**, **INVALID** or **NO RESULT** outcomes (2.81%, 95% CI 2.56-3.09). Of those, 355 specimens yielded valid results upon repeat assay (18 specimens were not retested). The overall valid reporting rate of the assay was 99.6% (14,729/14,790).

21.2 *Chlamydia trachomatis* Performance Results

Results from the Xpert CT Assay were compared to the patient infected status (PIS) algorithm for determination of sensitivity, specificity, and predictive values. Sensitivity and specificity for CT by gender, specimen type, and symptom status are shown in Table 7.

Table 7. Xpert CT Assay vs. Patient Infected Status for CT Detection

Specimen		Sx Status	n	TP	FP	TN	FN	Prev %	Sensitivity% (95 CI)	Specificity% (95 CI)	PPV% (95 CI)	NPV% (95 CI)
Female	PC-VS	Sym	1294	79	20	1195	0	6.1	100 (95.4-100)	98.4 (97.5-99.0)	79.8 (70.5-87.2)	100 (99.7-100)
		Asym	2472	121	11	2339	1	4.9	99.2 (95.5-100)	99.5 (99.2-99.8)	91.7 (85.6-95.8)	>99.9 (99.8-100)
		All	3766	200	31	3534	1	5.3	99.5 (97.3-100)	99.1 (98.8-99.4)	86.6 (81.5-90.7)	>99.9 (99.8-100)
	ES	Sym	1293	76	5	1209	3	6.1	96.2 (89.3-99.2)	99.6 (99.0-99.9)	93.8 (86.2-98.0)	99.8 (99.3-99.9)
		Asym	2464	117	11	2331	5	5.0	95.9 (90.7-98.7)	99.5 (99.2-99.8)	91.4 (85.1-95.6)	99.8 (99.5-99.9)
		All	3757	193	16	3540	8	5.4	96.0 (92.3-98.3)	99.6 (99.3-99.7)	92.3 (87.9-95.6)	99.8 (99.6-99.9)
	Urine	Sym	1292	84	4	1203	1	6.6	98.8 (93.6-100)	99.7 (99.2-99.9)	95.5 (88.8-98.7)	99.9 (99.5-100)
		Asym	2475	123	2	2347	3	5.1	97.6 (93.2-99.5)	99.9 (99.7-100)	98.4 (94.3-99.8)	99.9 (99.6-100)
		All	3767	207	6	3550	4	5.6	98.1 (95.2-99.5)	99.8 (99.6-99.9)	97.2 (94.0-99.0)	99.9 (99.7-100)
Male	Urine	Sym	706	120	2	581	3	17.4	97.6 (93.0-99.5)	99.7 (98.8-100)	98.4 (94.2-99.8)	99.5 (98.5-99.9)
		Asym	2730	73	5	2652	0	2.7	100.0 (95.1-100)	99.8 (99.6-99.9)	93.6 (85.7-97.9)	100 (99.9-100)
		All	3436	193	7	3233	3	5.7	98.5 (95.6-99.7)	99.8 (99.6-99.9)	96.5 (92.9-98.6)	99.9 (99.7-100)

TP=true positive, FP=false positive, TN=true negative, FN=false negative, ES=endocervical swab, PC-VS=patient-collected vaginal swab

21.3 Cycle Threshold (Ct) Frequency Distribution

Patient-collected vaginal swabs, endocervical swabs and urine specimens were collected from 3781 females and urine specimens were collected from 3444 males at 36 collection sites in the US and the UK. A total of 212 females and 196 males were infected with CT. The frequency distribution of Xpert CT Assay positive results for CT infected study subjects is shown in Figure 6.

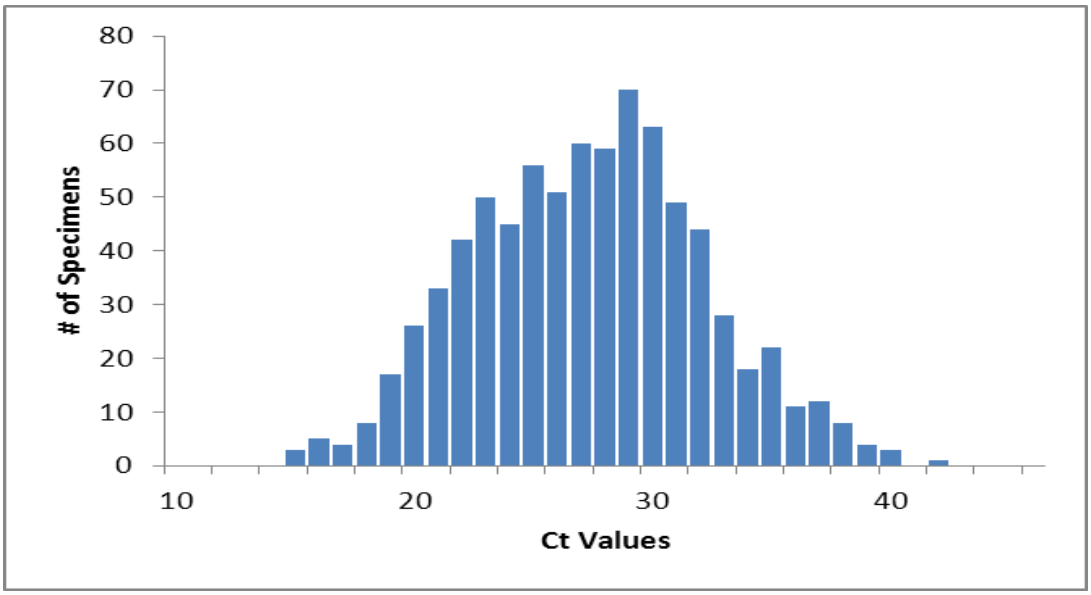

Figure 6. Ct Distribution of Patients Designated as Positive for CT Based on PIS Algorithm

Table 8 shows the number of results from symptomatic and asymptomatic females designated as infected or not infected with CT based on the PIS algorithm.

Table 8. Patient Infected Status – Female CT

PIS[a]	NAAT1		NAAT2		Xpert			Symptom Status		Total
	SW[a]	UR[a]	SW	UR	PC-VS[a]	ES[a]	UR	Symp	Asymp	
NI[b]	-	-	-	-	-	-	-	1160	2269	3429
NI	-	-	-	-	IND	-	-	6	8	14
NI	-	-	-	-	-	IND[c]	-	6	16	22
NI	-	-	-	-	-	-	IND	5	6	11
NI	-	-	-	-	+	+	-	0	1	1
NI	-	-	-	-	+	-	-	6	4	10
NI	-	-	-	-	-	+	-	3	5	8
NI	-	-	-	-	-	-	+	1	0	1
NI	-	-	-	EQ[d]	-	-	-	6	20	26
NI	-	-	-	EQ	IND	IND	-	1	0	1
NI	-	-	EQ	-	-	-	-	3	4	7
NI	-	-	EQ	-	-	-	IND	1	0	1
NI	-	-	-	+	-	-	-	0	7	7
NI	-	-	+	-	-	-	-	3	0	3
NI	-	-	+	-	-	+	-	0	1	1
NI[e]	-	+	-	+	+	-	+	7	1	8
NI[e]	-	+	-	+	+	-	-	0	1	1

Table 8. Patient Infected Status – Female CT (Continued)

PIS[a]	NAAT1		NAAT2		Xpert			Symptom Status		Total
	SW[a]	UR[a]	SW	UR	PC-VS[a]	ES[a]	UR	Symp	Asymp	
NI[e]	-	+	-	+	-	-	+	0	1	1
NI	-	+	-	-	-	-	-	1	0	1
NI	-	+	-	-	+	-	+	1	0	1
NI	+	-	-	-	-	-	-	4	8	12
NI	+	-	-	-	+	-	-	2	1	3
NI	+	-	-	-	+	+	-	1	2	3
NI	+	-	-	-	-	+	-	0	1	1
NI	+	+	-	-	-	-	-	1	0	1
NI	+	+	-	-	-	-	+	0	1	1
NI	+	+	-	-	+	+	+	1	1	2
NI	+	+	-	-	+	-	+	1	0	1
NI	+	+	-	-	+	-	-	1	0	1
Total Non-Infected								**1221**	**2358**	**3579**
I[f]	+	+	+	+	+	+	+	65	104	169
I	+	+	+	+	IND	+	+	0	1	1
I	+	+	+	+	+	IND	+	0	1	1
I	+	+	+	+	+	+	IND	1	0	1
I	+	+	+	+	-	+	+	0	1	1
I	+	+	+	+	+	-	+	0	1	1
I[e]	-	+	-	+	+	-	+	7	1	8
I[e]	-	+	-	+	+	-	-	0	1	1
I[e]	-	+	-	+	-	-	+	0	1	1
I	-	+	+	+	+	+	+	0	2	2
I	+	-	+	+	+	+	+	1	0	1
I	+	-	+	+	+	-	+	0	1	1
I	+	-	+	+	+	+	+	1	0	1
I	+	+	-	+	+	-	+	3	2	5
I	+	+	-	+	+	+	+	4	2	6
I	+	+	+	-	+	+	+	3	4	7
I	+	+	+	-	+	+	-	1	1	2
I	+	+	+	-	+	-	+	0	1	1
I	+	-	+	-	+	+	+	1	0	1
I	+	-	EQ	+	+	+	+	0	1	1
Total Infected								**87**	**125**	**212**

a. PIS = Patient Infected Status; SW = swab; UR = urine; PC-VS = patient-collected vaginal swab; ES = endocervical swab
b. NI = Non-infected
c. IND = Indeterminate – **ERROR**, **INVALID** or **NO RESULT** by Xpert CT Assay; specimens with IND results by Xpert are not included in the performance tables for that specimen type.
d. EQ = Equivocal result for this individual specimen type only; PIS status determined based on remaining specimens.
e. These samples are infected for urine and non-infected for swabs. In this table, they appear twice.
f. I = Infected

Table 9 shows the number of results from symptomatic and asymptomatic males designated as infected or not infected with CT based on the PIS algorithm.

Table 9. Patient Infected Status – Male CT

PIS[a]	NAAT1		NAAT2		GX	Symptom Status		Total
	SW[a]	UR[a]	SW	UR	UR	Symp	Asymp	
NI[b]	-	-	-	-	-	568	2621	3189
NI	-	-	-	EQ[c]	-	0	19	19
NI	-	-	+	-	-	2	1	3
NI	+	-	-	-	-	6	1	7
NI	+	+	-	-	-	1	1	2
NI	-	-	-	+	-	2	7	9
NI	-	+	-	-	-	2	1	3
NI	-	-	EQ	-	-	0	1	1
NI	+	+	-	-	+	2	4	6
NI	-	-	-	-	+	0	1	1
NI	-	-	-	-	IND[d]	1	6	7
NI	-	-	-	EQ	IND	0	1	1
Total Non-Infected						**584**	**2664**	**3248**
I[e]	+	+	+	+	+	104	50	154
I	+	+	-	+	+	8	10	18
I	-	+	-	+	+	4	7	11
I	+	+	+	-	+	2	2	4
I	+	-	+	-	+	1	0	1
I	+	-	-	+	+	1	0	1
I	-	+	+	+	+	0	1	1
I	+	+	+	EQ	+	0	2	2
I	EQ	+	-	+	+	0	1	1
I	+	-	+	-	-	2	0	2
I	+	+	+	-	-	1	0	1
Total Infected						**123**	**73**	**196**

a. PIS = Patient Infected Status; SW = Swab; UR = urine.
b. NI = Non-infected
c. EQ = Equivocal result for this individual specimen type only; PIS status determined based on remaining specimens.
d. IND = Indeterminate – **ERROR**, **INVALID** or **NO RESULT** by Xpert CT Assay; specimens with IND results by Xpert are not included in the performance tables for that specimen type.
e. I = Infected

22 Analytical Performance

22.1 Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert CT Assay with purified CT elementary bodies seeded into negative natural human pooled vaginal swab and pooled male urine matrices.

Pooled Vaginal Swab Matrix

Elementary bodies from two CT serovars, ATCC vr885 serovar D and ATCC vr879 serovar H, were purified by centrifugation through a 30% sucrose cushion and titered by enumeration of elementary bodies by transmission electron microscopy. Each serovar was diluted into pooled negative vaginal swab matrix and tested with the Xpert CT Assay. Replicates of 20 were evaluated at eight concentrations for CT serovar D and at seven concentrations for CT serovar H and LoDs were estimated by probit analysis. The claimed LoDs were confirmed by analyzing at least 20 replicate samples with elementary bodies diluted to the estimated LoD concentrations. For this study, the claimed LoD is defined as the lowest concentration at which 95% of at least 20 replicates are positive.

The claimed LoD for purified CT serovar D elementary bodies (EB) in vaginal swab matrix is 84 EB/mL. The claimed LoD for purified CT serovar H elementary bodies in vaginal swab matrix is 161 EB/mL (Table 10). In this study, LoDs for the remaining purified CT serovars (in EB/mL) are A (600), B (6), Ba (1900), C (34), E (6), F (202), G (96), I (21), J (150), K (117), LGV I (31), LGV II (20) and LGV III (210) EB/mL.

Table 10. LoD of Two CT Serovars in Pooled Vaginal Swab Matrix

Organism	LoD
CT ATCC vr885 serovar D (EB/mL)	84
CT ATCC vr879 serovar H (EB/mL)	161

Pooled Male Urine Matrix

Purified and titered elementary bodies from two CT serovars, ATCC vr885 serovar D and ATCC vr879 serovar H, were each tested in a sample matrix of negative pooled male urine. Replicates of 20 were evaluated at eight concentrations for CT serovar D and at seven concentrations for CT serovar H and LoDs were estimated by probit analysis. The claimed LoDs were confirmed by analyzing at least 20 replicate samples with elementary bodies diluted to the estimated LoD concentrations. For this study, the claimed LoD is defined as the lowest concentration at which 95% of at least 20 replicates are positive.

The claimed LoD for purified CT serovar D elementary bodies in male urine matrix is 75 EB/mL. The claimed LoD for purified CT serovar H elementary bodies in male urine matrix is 134 EB/mL (Table 11). In this study, LoDs for the remaining purified CT serovars (in EB/mL) are A (900), B (11), Ba (3037), C (34), E (12), F (151), G (48), I (43), J (112), K (88), LGV I (31), LGV II (40) and LGV III (157).

Table 11. LoD of Two CT Serovars in Pooled Male Urine Matrix

Organism	LoD
CT ATCC vr885 serovar D (EB/mL)	75
CT ATCC vr879 serovar H (EB/mL)	134

22.2 Analytical Specificity (Cross-reactivity)

One hundred and one (101) different microorganisms were tested at a concentration of at least 10^6 CFU/mL or 10^5 genome copies/mL in replicates of three (Table 12). All isolates were reported **CT NOT DETECTED**; none of the organisms were detected by the Xpert CT Assay. Positive and negative controls were included in the study. The analytical specificity was 100%.

Table 12. Potential Cross-Reacting Microorganisms in the Xpert CT Assay

Acinetobacter calcoaceticus	Herpes simplex virus I[1]	*Neisseria sicca (3)*
Acinetobacter lwoffi	Herpes simplex virus II[1]	*Neisseria subflava (2)*
Aerococcus viridans	Human papilloma virus[1]	*Paracoccus denitrificans*
Aeromonas hydrophila	*Kingella denitrificans*	*Peptostreptococcus anaerobius*
Alcaligenes faecalis	*Kingella kingae*	*Plesiomonas shigelloides*
Arcanobacterium pyogenes	*Klebsiella oxytoca*	*Propionibacterium acnes*
Bacteriodes fragilis	*Klebsiella pneumoniae*	*Proteus mirabilis*
Bifidobacterium adolescentis	*Lactobacillus acidophilus*	*Proteus vulgaris*
Branhamella catarrhalis	*Lactobacillus brevis*	*Providencia stuartii*
Brevibacterium linens	*Lactobacillus jensonii*	*Pseudomonas aeruginosa*
Candida albicans	*Lactobacillus lactis*	*Pseudomonas fluorescens*
Candida glabrata	*Legionella pneumophila*	*Pseudomonas putida*
Candida parapsilosis	*Leuconostoc paramensenteroides*	*Rahnella aquatilis*
Candida tropicalis	*Listeria monocytogenes*	*Saccharomyces cerevisiae*
Chlamydia pneumoniae	*Micrococcus luteus*	*Salmonella minnesota*
Chromobacterium violaceum	*Moraxella lacunata*	*Salmonella typhimurium*
Citrobacter freundii	*Moraxella osloensis*	*Serratia marcescens*
Clostridium perfringens	*Morganella morganii*	*Staphylococcus aureus*
Corynebacterium genitalium	*Mycobacterium smegmatis*	*Staphylococcus epidermidis*
Corynebacterium xerosis	*N. meningiditis*	*Staphylococcus saprophyticus*
Cryptococcus neoformans	*N. meningitidis Serogroup A*	*Streptococcus agalactiae*
Cytomegalovirus[1]	*N. meningitidis Serogroup B*	*Streptococcus bovis*
Eikenella corrodens	*N. meningitidis Serogroup C*	*Streptococcus mitis*
Entercoccus avium	*N. meningitidis Serogroup D*	*Streptococcus mutans*
Entercoccus faecalis	*N. meningitidis Serogroup W135*	*Streptococcus pneumoniae*
Entercoccus faecium	*N. meningitidis Serogroup Y*	*Streptococcus pyogenes*
Enterobacter aerogenes	*Neisseria cinerea*	*Streptococcus salivarius*
Enterobacter cloacae	*Neisseria dentrificans*	*Streptococcus sanguis*
Erysipelothrix rhusiopathiae	*Neisseria elongata (3)*	*Streptococcus griseinus*
Escherichia coli	*Neisseria flava*	*Vibrio parahaemolyticus*
Elizabethkingia meningoseptica[2]	*Neisseria flavescens (2)*	*Yersinia enterocolitica*
Fusobacterium nucleatum	*Neisseria lactamica (5)*	
Gardnerella vaginalis	*Neisseria mucosa (3)*	
Gemella haemolysans	*Neisseria perflava*	
Haemophilus influenzae	*Neisseria polysaccharea*	

(n) number of strains tested
[1] Tested at 1 x 10^5 genome copies/mL
[2] Previously known as *Flavobacterium meningosepticum*

22.3 Interfering Substances Study

Performance of the Xpert CT Assay was evaluated in the presence of potentially interfering substances. The evaluated substances were diluted into vaginal/endocervical swab simulated matrix and urine matrix containing either 5x LoD CT serovar D or 5x LoD CT serovar H.

There was no assay interference in the presence of the substances at the concentrations for vaginal/endocervical matrix (Table 13) and urine matrix (Table 14).

Table 13. Potentially Interfering Substances in Vaginal/Endocervical Matrix

Substance	Concentration
Blood	1.0% v/v
Mucin	0.8% w/v
Seminal Fluid	5.0% v/v
Hormones	7 mg/mL Progesterone + 0.07 mg/mL Beta Estradiol
LGV II (CT EB)	10^6 EB/mL
Vagisil Anti-Itch Cream	0.25% w/v
Clotrimazole Vaginal Cream	0.25% w/v
Preparation H Hemorroidal 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	0.25% w/v
Vagi Gard Moisturizing Gel	0.25% w/v
KY Jelly Personal Lubricant	0.25% w/v
Yeast Gard Douche	0.25% w/v
Delfen Vaginal Contraceptive Foam	0.25% w/v
VH Essentials Povidone-Iodine Medicated Douche	0.25% v/v
Leukocytes	10^6 cells/mL

Table 14. Potentially Interfering Substances in Urine Matrix

Substance	Concentration
Blood	0.3% v/v
Mucin	0.2% v/v
Seminal Fluid	5.0% v/v
Hormones	7 mg/mL Progesterone + 0.07 mg/mL Beta Estradiol
LGV II (CT EB)	10^6 EB/mL
Leukocytes	10^6 cells/mL
Norforms Deodorant Suppositories	0.25% w/v
BSA	10 mg/ml
Glucose	10 mg/mL
Bilirubin	0.2 mg/mL
Aspirin	40 mg/mL
Azithromycin	1.8 mg/mL
Doxycycline	3.6 mg/mL
Organisms - UTI *Candida albicans*/ *Staphylococcus aureus*/*Escherichia coli*	2.9 x 10^4 CFU/mL
Acetaminophen	3.2 mg/mL
Vagisil Feminine Powder	0.25% w/v
Acidic Urine	pH 4.0
Alkaline Urine	pH 9.0

With vaginal/endocervical specimens, assay interference may be observed in the presence of:

- Blood at a concentration greater than 1% v/v;
- Mucin at a concentration greater than 0.8% w/v.

With urine specimens, assay interference may be observed in the presence of:

- Blood at a concentration greater than 0.3% v/v;
- Mucin at a concentration greater than 0.2% w/v;
- Bilirubin at a concentration greater than 0.2 mg/mL (20 mg/dL);
- Vagisil feminine powder at a concentration greater than 0.2% w/v.

22.4 Carry-Over Contamination Study

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination in negative samples run following very high positive samples in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately following a sample with high CT spike (1.9 x 10^4 EB/mL). Two sample types were used for this testing: a) known pooled negative urine samples; and b) known pooled negative swab samples. Each sample type was tested in each of four GeneXpert modules for a total of 44 runs resulting in 20 positives and 24 negatives. All 40 positive samples were correctly reported as **CT DETECTED**. All 48 negative samples were correctly reported as **CT NOT DETECTED**.

22.5 Reproducibility

Reproducibility of the Xpert CT Assay was evaluated at three sites using specimens comprised of CT organisms seeded into pooled, negative male urine or pooled, negative female vaginal swab samples. The specimens were prepared at concentration levels representing low positive (1X LoD), moderate positive (2-3X LoD), and high positive (>20X LoD) for each organism. Negative panel members were also included, and were comprised of pooled, negative male urine and pooled, negative vaginal swab samples. A panel of 22 specimens (11 in urine matrix and 11 in swab matrix) was tested on five different days by two different operators four times per day at three sites (22 specimens x 2 operators x 5 days x 4 replicates per day x 3 sites). Three lots of Xpert CT reagents were included in the study, with two lots being tested at each site. Xpert CT Assays were performed according to the Xpert CT Assay procedure. The rate of agreement with expected results of CT for each panel member is shown by site in Table 15 and Table 16.

Table 15. Summary of Reproducibility Results by Study Site; Percent Agreement Swab Samples

Sample	Site 1 (GeneXpert Dx)	Site 2 (Infinity-80)	Site 3 (Infinity-48)	% Total Agreement by Sample
CT >20X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT >20X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT >20X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 1X LoD	90.0% (36/40)	97.5% (39/40)	95.0% (38/40)	94.2% (113/120)
CT 1X LoD	97.5% (39/40)	100% (40/40)	100% (40/40)	99.2% (119/120)
CT 1X LoD	97.5% (39/40)	90.0% (36/40)	90.0% (36/40)	92.5% (111/120)
CT 2-3X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)

Table 16. Summary of Reproducibility Results by Study Site; Percent Agreement Urine Samples

Sample	Site 1 (GeneXpert Dx)	Site 2 (Infinity-80)	Site 3 (Infinity-48)	% Total Agreement by Sample
CT >20X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT >20X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT >20X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 1X LoD	92.5% (37/40)	95.0% (38/40)	90.0% (36/40)	92.5% (111/120)
CT 1X LoD	95.0% (38/40)	80.0% (32/40)	87.5% (35/40)	87.5% (105/120)
CT 1X LoD	87.5% (35/40)	97.5% (39/40)	97.5% (39/40)	94.2% (113/120)
CT 2-3X LoD	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg	97.5% (39/40)	100% (40/40)	100% (40/40)	99.2% (119/120)
CT neg	100% (40/40)	100% (40/40)	97.5% (39/40)	99.2% (119/120)
CT neg	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg	100% (40/40)	100% (40/40)	97.5% (39/40)	99.2% (119/120)

The reproducibility of the Xpert CT 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, and between-runs for each panel member are shown in Table 17 through Table 20.

Table 17. Summary of Reproducibility Data for Swab and Urine Specimens – CT1 Target

Type	Target Conc.				Between-Site		Between- Lot		Between-Day		Between-Run[a]		Within-Run		Total	
	CT (LoD)	Agree/N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	120/120	100	20.67	0.21	1.0	0.11	0.5	0.11	0.5	0.00	0.0	0.29	1.4	0.39	1.9
	>20X	112/120	93.3	20.73	0.29	1.4	0.37	1.8	0.00	0.0	0.00	0.0	1.59	7.7	1.66	8.0
	>20X	120/120	100	20.59	0.00	0.0	0.21	1.0	0.06	0.3	0.08	0.4	0.26	1.3	0.35	1.7
	1X	113/120	94.2	37.20	0.10	0.3	0.21	0.6	0.00	0.0	0.00	0.0	1.15	3.1	1.18	3.2
	1X	106/120	88.3	37.04	0.17	0.5	0.00	0.0	0.00	0.0	0.12	0.3	1.08	2.9	1.10	3.0
	1X	111/120	92.5	37.04	0.06	0.2	0.00	0.0	0.00	0.0	0.00	0.0	1.12	3.0	1.12	3.0
	2-3X	120/120	100	35.63	0.13	0.4	0.00	0.0	0.15	0.4	0.10	0.3	0.77	2.2	0.80	2.3
	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	118/120	98.3	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	120/120	100	21.46	0.23	1.0	0.00	0.0	0.12	0.5	0.02	0.1	0.31	1.4	0.40	1.9
	>20X	115/120	95.8	21.33	0.13	0.6	0.05	0.2	0.13	0.6	0.00	0.0	0.43	2.0	0.47	2.2
	>20X	120/120	100	21.36	0.19	0.9	0.00	0.0	0.12	0.6	0.02	0.1	0.47	2.2	0.52	2.4
	1X	111/120	92.5	37.24	0.36	1.0	0.00	0.0	0.00	0.0	0.00	0.0	1.33	3.6	1.38	3.7
	1X	97/120	80.8	37.15	0.40	1.1	0.18	0.5	0.17	0.4	0.00	0.0	1.02	2.8	1.13	3.0
	1X	113/120	94.2	37.39	0.10	0.3	0.32	0.9	0.00	0.0	0.00	0.0	1.38	3.7	1.42	3.8
	2-3X	120/120	100	35.26	0.24	0.7	0.00	0.0	0.30	0.9	0.00	0.0	0.80	2.3	0.89	2.5
	NEG	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	118/120	98.3	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

a. A run is defined as the four samples per panel member run by one operator at one site on one day.

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation, N/A=Not Applicable for negative samples, SD=standard deviation

Note Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

23 Instrument System Precision

An in-house precision study was conducted to compare the performance of the GeneXpert Dx and the Infinity-80 Instrument Systems using specimens comprised of CT organisms seeded into negative urine or simulated vaginal swab matrix. The specimens were prepared at concentration levels representing low positive (0.25-0.5X LoD), moderate positive (2-3X LoD), and high positive (>20X LoD) for each organism. Negative panel members were also included and were comprised of negative urine and negative diluent. A panel of 20 specimens (10 in urine matrix and 10 in 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 two instrument systems (20 specimens x 4 times/ day x 12 days x 2 operators x 2 instrument systems). One lot of Xpert CT Assay was used for the study. Xpert CT assays were performed according to the Xpert CT Assay procedure. The rate of agreement with expected results of CT for each panel member is shown by instrument in Table 18 and Table 19.

Table 18. Summary of Instrument System Precision Results; Percent Agreement Swab Matrix

Sample	GeneXpert Dx	Infinity-80	% Total Agreement by Sample
CT >20X LoD	100% (96/96)	100% (95/95)[a]	100% (191/191)
CT >20X LoD	100% (96/96)	100% (96/96)	100% (192/192)
CT >20X LoD	100% (96/96)	100% (95/95)[b]	100% (191/191)
CT 0.25-0.5X LoD	46.9% (45/96)	42.7% (41/96)	44.8% (86/192)
CT 0.25-0.5X LoD	55.2% (53/96)	60.4% (58/96)	57.8% (111/192)
CT 0.25-0.5X LoD	61.5% (59/96)	62.1% (59/95)[c]	61.8% (118/191)
CT 2-3X LoD	100% (96/96)	100% (96/96)	100% (192/192)
CT neg	100% (96/96)	100% (96/96)	100% (192/192)
CT neg	100% (95/95)[b]	100% (96/96)	100% (191/191)
CT neg	100% (96/96)	100% (96/96)	100% (192/192)

a. One sample was indeterminate after initial and retest.
b. One sample each of CT >20X LoD and CT neg resulted in **ERROR** on initial test and were not retested.
c. One sample mistakenly not tested.

Table 19. Summary of Instrument System Precision Results; Percent Agreement Urine Matrix

Sample	GeneXpert Dx	Infinity-80	% Total Agreement by Sample
CT >20X LoD	100% (96/96)	100% (96/96)	100% (192/192)
CT >20X LoD	100% (96/96)	100% (96/96)	100% (192/192)
CT >20X LoD	100% (96/96)	100% (96/96)	100% (192/192)
CT 0.25-0.5X LoD	50.0% (48/96)	52.1% (50/96)	51.0% (98/192)
CT 0.25-0.5X LoD	44.8% (43/96)	39.6% (38/96)	42.2% (81/192)
CT 0.25-0.5X LoD	46.9% (45/96)	46.9% (45/96)	46.9% (90/192)
CT 2-3X LoD	100% (96/96)	100% (96/96)	100% (192/192)
CT neg	100% (96/96)	100% (96/96)	100% (192/192)
CT neg	100% (96/96)	100% (96/96)	100% (192/192)
CT neg	100% (96/96)	100% (96/96)	100% (192/192)

The precision of the Xpert CT 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-days, and between-runs for each panel member are shown in Table 20.

Table 20. Summary of Precision Data for Swab and Urine Specimens – CT1 Target

Type	Target Conc.				Between-Instrument		Between- Day		Between-Run[a]		Within-Run		Total	
	CT (LoD)	Agree/ N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	191/191	100	23.52	0.05	0.2	0.02	0.1	0.00	0.0	0.25	1.1	0.26	1.1
	>20X	110/192	57.3	23.52	0.00	0.0	0.00	0.0	0.08	0.3	0.18	0.7	0.19	0.8
	>20X	191/191	100	23.55	0.03	0.1	0.00	0.0	0.00	0.0	0.22	0.9	0.22	0.9
	0.25-0.5X	86/192	44.8	38.77	0.00	0.0	0.00	0.0	0.32	0.8	1.38	3.6	1.42	3.7
	0.25-0.5X	59/192	30.7	38.46	0.00	0.0	0.30	0.8	0.00	0.0	1.35	3.5	1.39	3.6
	0.25-0.5X	118/191	61.8	38.05	0.08	0.2	0.00	0.0	0.00	0.0	1.26	3.3	1.26	3.3
	2-3X	192/192	100	31.49	0.04	0.1	0.00	0.0	0.06	0.2	0.24	0.8	0.25	0.8
	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	116/191	60.7	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	192/192	100	24.35	0.05	0.2	0.20	0.8	0.10	0.4	0.30	1.2	0.38	1.6
	>20X	92/192	47.9	24.25	0.00	0.0	0.06	0.3	0.00	0.0	0.62	2.6	0.62	2.6
	>20X	192/192	100	24.12	0.00	0.0	0.15	0.6	0.19	0.8	0.34	1.4	0.41	1.7
	0.25-0.5X	98/192	51.0	38.33	0.12	0.3	0.00	0.0	0.84	2.2	1.03	2.7	1.33	3.5
	0.25-0.5X	48/192	25.0	38.26	0.00	0.0	0.00	0.0	0.56	1.5	1.05	2.7	1.19	3.1
	0.25-0.5X	90/192	46.9	38.39	0.00	0.0	0.00	0.0	0.00	0.0	1.09	2.8	1.09	2.8
	2-3X	192/192	100	31.85	0.00	0.0	0.11	0.4	0.18	0.6	0.32	1.0	0.39	1.2
	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	67/192	34.9	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

a. A run is defined as the four samples per panel member run by one operator at one site on one day.

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation, N/A=Not Applicable for negative samples, SD=standard deviation

Note Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

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25 Cepheid Headquarters Locations

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26 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

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

27 Table of Symbols

Symbol	Meaning
	Catalog number
	For In vitro Diagnostic Use
	Do not reuse
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <n> tests
	Control
	Expiration date
	CE marking – European Conformity
	Authorized Representative in Switzerland
	Importer
	Temperature limitation
	Biological risks
	Warning

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