

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K151565

B. Purpose for Submission:

The purpose of this submission is to show that the Cepheid[®] Xpert[®] *Trichomonas vaginalis* (TV) Assay on the Cepheid GeneXpert Instrument Systems (GeneXpert Dx, GeneXpert Infinity-48, GeneXpert Infinity-48s, and GeneXpertInfinity-80 systems) is substantially equivalent to the Gen-Probe APTIMA[®] *Trichomonas vaginalis* Assay on the PANTHER[®] System.

C. Measurand:

Trichomonas vaginalis (TV) DNA

D. Type of Test:

Real-time polymerase chain reaction (PCR)

E. Applicant:

Cepheid

F. Proprietary and Established Names:

Proprietary Name: Xpert[®] TV

Common Names: Xpert TV Assay, Xpert Trichomonas Assay

G. Regulatory Information:

1. Regulation section:

21 CFR 866.3860, *Trichomonas vaginalis* nucleic acid assay

2. Classification:

Class II

3. Product code:

OUI, OOI

4. Panel:

Microbiology (83)

H. Intended Use:

1. Intended use(s):

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 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.

Ancillary Collection Kits:

Xpert Vaginal/Endocervical Specimen Collection Kit

The Cepheid® Xpert® Vaginal/Endocervical Specimen Collection Kit is designed to collect, preserve, and transport *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* DNA in endocervical swab specimens (collected by a clinician) and patient-collected vaginal swab specimens (collected in a clinical setting) from symptomatic and asymptomatic women prior to analysis with the Xpert CT/NG Assay and the Xpert TV Assay.

Xpert Urine Specimen Collection Kit

The Cepheid® Xpert® Urine Specimen Collection Kit is designed to preserve and transport *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* DNA in first-catch urine specimens from symptomatic and asymptomatic individuals prior to analysis with the Xpert CT/NG Assay and the Xpert TV Assay. The Xpert Urine Specimen Collection Kit is intended for use with male (Xpert CT/NG Assay) and female (Xpert CT/NG Assay and Xpert TV Assay) urine.

2. Indication(s) for use:

Same as intended use

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

The Cepheid Xpert TV Assay uses PCR technology on the GeneXpert Instrument Systems,

which extract, amplify, and detect the target DNA.

I. Device Description:

The Xpert TV Assay is an automated real-time polymerase chain reaction (PCR) *in vitro* diagnostic test for qualitative detection of genomic DNA from *Trichomonas vaginalis*. The Xpert TV Assay is intended as an aid in the diagnosis of trichomoniasis.

The Xpert TV Assay is performed on the Cepheid GeneXpert® Instrument Systems (GeneXpert Dx, GeneXpert Infinity-48, GeneXpert Infinity-48s, and GeneXpert Infinity-80 systems). The GeneXpert Instrument System consists of an instrument, personal computer, and preloaded software for running tests and viewing the results. The GeneXpert Instrument System requires single-use, disposable cartridges (the Xpert TV cartridges) that hold the PCR reagents and host the PCR process. The cartridges are self-contained, so specimens never come into contact with the working parts of the instrument.

A Sample Processing Control (SPC), Sample Adequacy Control (SAC), and a Probe Check Control (PCC) are controls utilized by the GeneXpert Instrument System. The SPC is present to control for adequate processing of the target trichomonads and to monitor the presence of inhibitors in the real-time PCR reaction to reduce the possibility of false negative results. 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, real-time PCR tube filling in the cartridge, probe integrity, and dye stability.

The ancillary specimen collection kits for use with the Xpert TV Assay are the Cepheid Xpert Vaginal/Endocervical Specimen Collection Kit and the Cepheid Xpert Urine Specimen Collection Kit. The swab and/or urine specimens are collected from asymptomatic or symptomatic patients and placed into a specimen transport tube containing preservative. After transferring the specimen to the sample chamber of the Xpert TV cartridge, the user initiates a test, and places the cartridge into the GeneXpert Instrument System. Results are automatically generated by the instrument at the end of the process in a report that can be viewed and printed.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Gen-Probe® APTIMA *Trichomonas vaginalis* Assay on the PANTHER System.

2. Predicate 510(k) number(s):

K122062

3. Comparison with predicate:

Similarities		
Item	<u>Subject Device:</u> Cepheid Xpert TV Assay (K151565)	<u>Predicate Device:</u> Gen-Probe APTIMA <i>Trichomonas vaginalis</i> Assay (K122062)
Intended Use	<p>The Cepheid Xpert TV Assay, performed on the GeneXpert[®] Instrument Systems, is a qualitative <i>in vitro</i> diagnostic test for the detection of <i>Trichomonas vaginalis</i> genomic DNA. The test utilizes automated real-time polymerase chain reaction (PCR) to detect <i>Trichomonas vaginalis</i> genomic DNA. The Xpert TV Assay uses female 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.</p> <p>Ancillary Collection Kits:</p> <p>Xpert Vaginal/Endocervical Specimen Collection Kit</p> <p>The Cepheid[®] Xpert[®] Vaginal/Endocervical Specimen Collection Kit is designed to collect, preserve, and transport <i>Chlamydia trachomatis</i>, <i>Neisseria gonorrhoeae</i>, and <i>Trichomonas vaginalis</i> DNA in endocervical swab specimens (collected by a clinician) and patient-collected vaginal swab specimens (collected in a clinical setting) from symptomatic and asymptomatic women prior to analysis with the Xpert CT/NG Assay and the Xpert</p>	<p>The APTIMA <i>Trichomonas vaginalis</i> Assay is an <i>in vitro</i> qualitative nucleic acid amplification test (NAAT) for the detection of ribosomal RNA (rRNA) from <i>Trichomonas vaginalis</i> to aid in the diagnosis of trichomoniasis using the PANTHER System.</p> <p>The assay may be used to test the following specimens from symptomatic or asymptomatic women: clinician-collected endocervical swabs, clinician-collected vaginal swabs, and specimens collected in PreservCyt Solution.</p>

Similarities		
Item	<u>Subject Device:</u> Cepheid Xpert TV Assay (K151565)	<u>Predicate Device:</u> Gen-Probe APTIMA <i>Trichomonas vaginalis</i> Assay (K122062)
	<p>TV Assay.</p> <p>Xpert Urine Specimen Collection Kit</p> <p>The Cepheid® Xpert® Urine Specimen Collection Kit is designed to preserve and transport <i>Chlamydia trachomatis</i>, <i>Neisseria gonorrhoeae</i>, and <i>Trichomonas vaginalis</i> DNA in first-catch urine specimens from symptomatic and asymptomatic individuals prior to analysis with the Xpert CT/NG Assay and the Xpert TV Assay. The Xpert Urine Specimen Collection Kit is intended for use with male (Xpert CT/NG Assay) and female (Xpert CT/NG Assay and Xpert TV Assay) urine.</p>	
Assay Results	Qualitative	Same as predicate
Specimen Types	Endocervical Swabs Female Urine	Endocervical Swabs Female Urine
Differences		
Item	<u>Subject Device:</u> Cepheid Xpert TV Assay (K151565)	<u>Predicate Device:</u> Gen-Probe APTIMA <i>Trichomonas vaginalis</i> Assay (K122062)
Assay Target	<i>T. vaginalis</i> genomic DNA	<i>T. vaginalis</i> ribosomal RNA
Technology	Real-time polymerase chain reaction (PCR)	Transcription-mediated amplification (TMA)
Instrument System	Cepheid GeneXpert Instrument System	PANTHER Instrument System
Specimen Types	Patient-Collected Vaginal Swabs	Clinician-Collected Vaginal Swabs

K. Standard/Guidance Documents Referenced (if applicable):

1. FDA. *Format for Traditional and Abbreviated 510(k)s*. Guidance for Industry and FDA Staff; 2005.
2. FDA. *Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Systems*. Guidance for Industry and FDA Staff; 2005.
3. FDA. *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*. Guidance for Industry and FDA Staff; 2005.
4. FDA. *Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable*. Guidance for Industry and FDA Staff; 2006.
5. FDA. *Off-The-Shelf Software Use in Medical Devices*. Guidance for Industry and FDA Staff; 1999.
6. FDA. *Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software*. Guidance for Industry and FDA Staff; 2005.
7. FDA. *General Principles of Software Validation*. Guidance for Industry and FDA Staff; 2002.
8. FDA. *Content of Premarket Submissions for Management of Cybersecurity in Medical Devices*. Guidance for Industry and FDA Staff; 2014.
9. FCC. Part 15 (Subparts A and B) and Part 18.
10. CLSI MM03-A2: *Molecular Diagnostics Methods for Infectious Disease – Second Edition*; 2006.
11. CLSI EP17-A2, *Protocols for Determination of Limits of Detection and Limits of Quantitation, Approved Guideline – Second Edition*; 2006.
12. CLSI EP7-A2, *Interference Testing in Clinical Chemistry, Approved Guideline – Second Edition*; 2004.
13. CLSI EP15-A2, *User Verification of Performance for Precision and Trueness, Approved Guideline - Second Edition*; 2006.
14. CLSI *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition*; 2004.
15. ISO 10993: *Biological Evaluation of Medical Devices –Parts 1 (2009),7 (2008), and 10; 2010*.
16. ISO 11135-1: *Sterilization of Health Care Products – Ethylene Oxide – Part 1*; 2007.
17. ISO 11137-2: *Sterilization of Health Care Products – Radiation – Part 2*; 2013.
18. ASTM D4169: *Standard Practice for Performance Testing of Shipping Containers and Systems*; 2009.
19. EN 13640: *Stability Testing of in Vitro Diagnostic Reagents*; 2002.
20. EN 61326-1: *Electrical Equipment for Measurement and Control and Laboratory Use – Parts 1, 2, and 6*; 2006.
21. EN 61010: *Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use – Parts 1 (2001) and 2 (2002)*.
22. EN 55011: *Industrial, Scientific, and Medical Radio-Frequency Equipment – Electromagnetic Disturbance Characteristics*; 2007.
23. NF EN ISO 10993-5: *Biological Evaluation of Medical Devices – Part 5*; 2010.
24. UNI EN 556-1: *Sterilization of Medical Devices – Requirements for Medical Devices to be Designated “Sterile”*; 2002

25. IEC 61010: *Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use* – Parts 1 (2001) and 2-101; 2002.
26. CISPR 11: *Industrial, Scientific, and Medical Equipment-Radio Frequency Equipment-Electromagnetic Disturbance Characteristics*; 2004.
27. CISPR 22: *Information Technology Equipment-Radio Disturbance Characteristics – Limits and Methods of Measurement*; 2006.
28. CAN/CSA C22.2, No. 61010: *Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use* – Parts 1 and 2-101; 2004.
29. EMC Directive 2004/108/EC.
30. WEEE Directive 2002/96/EC.
31. LVD Directive 2006/95/EC.

L. Test Principle:

This is a nucleic acid based test using real-time PCR. *T. vaginalis* is detected through the use of real-time PCR to amplify and detect TV DNA. Genomic TV DNA is amplified and detected using a sequence-specific probe that is cleaved during PCR amplification, resulting in a signal that occurs when the fluorescent reporter dye is released from the quencher.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

- a. *Precision/Reproducibility:*

Reproducibility

A panel of 8 specimens with varying concentrations of TV (ATCC 30001) was tested on twelve non-consecutive days by two different operators, at each of three sites (8 specimens x 2 operators x 2 runs per day x 12 days x 3 sites = 1152 measurements total). Two runs were performed per day by each of the 6 study operators (12 days x 2 runs per day = 24 runs per operator). Each site used a different GeneXpert Instrument (running the same analytical software) for the analysis. Site 1 used an Infinity-80 instrument. Sites 2 and 3 used GeneXpert Dx instruments. The specimen panel was prepared in clinical matrix (either pooled vaginal swabs or urine in their respective Cepheid transport reagent). The panel consisted of four concentration levels per matrix: a high negative sample with an analyte concentration below the limit of detection (LoD), an LoD sample with an analyte concentration of 1X LoD, a moderate positive sample with an analyte concentration of 3X LoD, and a negative sample which was comprised of matrix only. Three lots of Xpert TV Assay cartridges were used at each of the 3 testing sites, with each lot being used for 4 days of testing. One TV positive and one negative control were tested daily prior to testing the panel specimens (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). Results are presented in Table 1.

Table 1. Reproducibility of the 8 Member Specimen Panel

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)
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 was indeterminate on initial testing and was retested.

The reproducibility of the Xpert TV Assay was also evaluated in terms of the fluorescent signal (expressed in Ct values) for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between sites, between days, and between operators for each panel member are presented in Table 2.

Table 2. Reproducibility of the Fluorescent Signal

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.

The data presented in Tables 1 and 2 demonstrate good reproducibility for the Xpert TV Assay on the GeneXpert Instrument Systems. The assay shows $\geq 88.8\%$ detection of TV in LoD samples diluted in pooled vaginal swab and urine matrix (detection in LoD samples is 93.1% if operator 1 from site 1 is excluded). Due to the relatively low LoD concentrations of TV analyte, it is believed that small variations in sample aliquots contributed to detection levels below the anticipated 95%.

Detection of TV was 100% for moderate positive samples diluted in pooled vaginal swab and urine matrix. Detection was $\leq 76.4\%$ for the high negative samples, which is acceptable and typical for real-time PCR assays.

Agreement between all operators was evaluated using Fisher's Exact test to assess operator performance. No statistically significant differences were observed for any of the specimens (including the Urine LoD sample; p-value =0.061). Therefore, the operator performance was deemed acceptable. Detection was $\leq 76.4\%$ for the high negative samples, which is acceptable and typical for real-time PCR assays.

Instrument Precision

An in-house precision study was conducted to compare the performance of the GeneXpert Dx and the GeneXpert Infinity Instrument Systems. A panel of 8 specimens with varying concentrations of TV was tested on 12 different days by two operators. Each operator conducted four runs of the specimen panel per day on three different instruments (8 specimens x 12 days x 2 operators x 4 runs per day x 3 instrument systems = 2304 measurements total). The three instruments included in this study were the GeneXpert Dx, the Infinity-48, and the Infinity-80 (running the same analytical software). Three lots of Xpert TV Assay cartridges were used for the study, each lot used for 4 days of testing. One TV positive and one negative control were tested daily prior to testing the panel specimens (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). Results are summarized in Table 3.

Table 3. In-House Precision for the 8 Member Specimen Panel

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 fluorescent 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 4.

Table 4. Precision of the Fluorescent Signal

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.

The data presented in Tables 3 and 4 demonstrated acceptable precision between instruments as it shows 100% detection for TV diluted in swab or urine matrix at the moderate positive level on all three instruments. Detection of samples at the assay LoD was $\geq 91.7\%$ for both matrices. Due to the relatively low LoD concentrations of TV analyte, it is believed that small variations in sample aliquots contributed to detection levels below the anticipated 95%.

b. Linearity/assay reportable range:

N/A

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

External Controls

The external positive control (ZeptoMetrix; Catalog # NATTVPOS-6MC) for the Xpert TV Assay consists of NATtrol inactivated and heat-treated cells of TV strain Z070 and human A549 cells. The external negative control (ZeptoMetrix; Catalog # NATTVNEG-6MC) consists of NATtrol inactivated cells of *Neisseria gonorrhoeae* strain Z017 and human A549 cells. Three

lots of these controls were tested in replicates of six (positive external control) or four (negative external control). Of the 33 runs, all 18 runs with positive controls were reported as “TV DETECTED” by the Xpert TV Assay. Of the 12 runs with negative controls, 11 were reported as “TV NOT DETECTED” and one provided an indeterminate GeneXpert result (ERROR). To verify that *N. gonorrhoeae* cells were present in the three negative control lots tested, a single sample from each of the lots was taken tested in triplicate using the Xpert CT/NG Assay. All three runs were reported as “CT NOT DETECTED, NG DETECTED.” These results indicate that the external controls gave the expected results using the Xpert TV Assay.

Internal Controls

The Xpert TV Assay includes the following internal controls: Sample Adequacy Control (SAC), Sample Processing Control (SPC), and the Probe Check Control (PCC).

1. Sample Adequacy Control (SAC): The SAC verifies that human DNA is present in the sample, indicating that sample collection was adequate. Test results are reported as “INVALID” if the SAC fails to meet the valid minimum or maximum Ct specification (range 9-45 Ct). Examination of all SAC values obtained from samples tested in the clinical study indicated that, out of 5391 total runs for eligible specimens, two samples (0.037%) received a GeneXpert result of “INVALID.” Both were due to SAC failure. In addition, examination of the SAC Ct values of the 4744 samples that were negative relative to the patient infected status, indicated that none of the Ct values obtained from clinical samples with valid Xpert TV Assay results approached the SAC maximum cycle cut-off of Ct 45. This data indicates that the Ct range for the SAC is appropriate and that the SAC functions as an adequate control for sample adequacy.
2. Sample Processing Control (SPC): The SPC bead contains genomic DNA of *Bacillus globigii* that is included in each cartridge to verify adequate processing of the sample. The SPC is processed with the sample and verifies the effectiveness of each sample preparation step including; binding and elution of DNA, correct reaction tube filling, PCR components are present and functioning, and monitors the presence of potential inhibitor(s) in the real-time PCR assay. Test results are reported as “INVALID” if the SPC fails to meet the valid minimum or maximum Ct specification (range 9-45 Ct). From 5391 eligible samples tested during the clinical study, zero “INVALID” GeneXpert results were due to an SPC failure alone and zero “INVALID” GeneXpert results were caused by failure of both the SAC and SPC. In addition, examination of the SPC Ct values of the 4744 samples that were negative relative to the patient infected status, indicated that none of the Ct values obtained from clinical samples with valid Xpert TV Assay results approached the SPC maximum cycle cut-off of Ct 45. This data indicates that the Ct range for the SPC is appropriate and that the SPC functions as an adequate control to monitor nucleic acid extraction and amplification.
3. Probe Check Control (PCC): After sample preparation, bead reconstitution, and reaction tube filling, but prior to thermal cycling, the GeneXpert Instrument System is programmed to perform a probe check on the amplification mixture. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability. The PCC is considered to PASS if the fluorescence generated meets the validated acceptance criteria. If the PCC fails for the TV target or the SAC and SPC controls, a

probe check error is reported and the test will not continue. If a probe check error is reported, the test may be repeated using a new sample, a new cartridge, and new reagents. During clinical testing, one test result was reported as “ERROR” due to a PCC failure out of 5391 total runs for eligible specimens (0.02%).

Shipping and Storage Stability

The conditions claimed for specimen transport and storage were evaluated for first-catch urine, endocervical swabs, and patient-collected vaginal swabs (collected in a clinical setting). Cultured and titered TV cells (strain ATCC 30001) were spiked into pooled negative urine or swab specimens (in their respective Cepheid transport reagent) at a concentration of 3X LoD. One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). The data for this study was collected with the GenXpert Dx (GX-IV and GX-XVI) Instrument. For the TV positive samples, replicates of 16 were tested at t = 0 and replicates of 8 were tested at all other time and temperature combinations. For the TV negative samples (matrix only), replicates of 8 were tested at t = 0 and replicates of 4 were tested at all other time and temperature combinations.

- Pooled negative urine in Cepheid transport reagent was stored at 2°C and 8°C and tested at selected time points up to 61 days (t = 0, 7, 14, 28, 42, and 61 days), or stored at 15°C and 30°C and tested at selected time points up to 28 days (t = 0, 7, 14, 21, and 28 days).
- Pooled unpreserved urine was stored at 2°C and 8°C, and tested at selected time points up to 7 days (t = 0, 1, 4, and 7 days), or stored at 15°C and 30°C, and tested at selected time points up to 7 hours (t = 0, 2, 4, and 7 hours).
- Pooled vaginal or endocervical swabs stored in Cepheid transport reagent were stored at 2°C and 30°C and tested at selected time points up to 61 days (t = 0, 14, 28, and 61 days).

The results of this study support the following claims for specimen shipping and storage:

- Female urine in Xpert Urine Transport Reagent refrigerated at 2-8°C for 28 days or at 15-30°C (room temperature) for 14 days.
- Vaginal and endocervical swabs in Xpert Swab Transport Reagent at 2-30°C for 60 days.
- Female urine neat (no preservative) refrigerated at 2-8°C for 4 days or at 15-30°C for 4 hours.

Specimen Stability – Cartridge Hold Time Study

If an Xpert cartridge is loaded onto a fully loaded GeneXpert Infinity Instrument, samples may wait up to two hours before a GenXpert module becomes available. During this wait time, the assay target organisms and human cells may degrade or become unstable, resulting in a low positive (“NEGATIVE”) or invalid (SAC Ct not within the valid range) result.

The cartridge hold time study was conducted to determine the acceptable maximum hold time for Xpert TV Assay cartridges held on the GeneXpert Infinity System. Cultured and titered TV cells (strain ATCC 30001) and human A549 cells were spiked into pooled negative urine or vaginal swab specimens (in their respective Cepheid transport reagent) at a concentration of 3X LoD and as a 10X high positive cell mix, respectively. Samples loaded into Xpert TV cartridges were

tested after incubation for 1, 4, or 5 hours at ambient conditions (room temperature and ambient humidity), high humidity (25°C and 75% relative humidity), and at high temperature (35°C and ambient humidity). Replicates of 8 positive and 8 negative samples (human A549 cells and matrix only) were tested at each of the time and temperature combinations. One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells, respectively). The data for this study was collected with the GenXpert Dx (GX-IV and GX-XVI) Instruments. Xpert TV Assay cartridges were held at three storage conditions (room temperature, 25°C/75% relative humidity, and 35°C) and tested at t = 0, 1, 4, and 5 hours. Positive and negative samples were tested in replicates of eight.

The results of this study support the following claims for on-board specimen storage:

- Urine and swabs in Cepheid transport reagent loaded into Xpert TV cartridges can be stored on-board the GeneXpert Infinity for up to 4 hours prior to testing with the Xpert TV Assay.

d. Detection limit:

Limit of Detection (LoD)

LoD was established using two TV strains, one metronidazole sensitive (ATCC 30001) and one metronidazole resistant (ATCC 30238) diluted into negative clinical matrix (either pooled vaginal swabs or urine in their respective Cepheid transport reagent). The LoD is defined as the lowest concentration (expressed as number of cells per milliliter; cells/ml) per sample that can be reproducibly distinguished from negative samples with 95% confidence or the lowest concentration at which 19 of 20 replicates were positive. Each strain was initially tested in a range finding study at 5 different concentrations in replicates of 20 per concentration of TV. Testing was performed with two lots of reagents across three testing days. One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). The data for this study was collected with the GenXpert Dx (GX-IV and GX-XVI) and the GeneXpert Infinity-80 Instruments. The results of the LoD range finding study are shown in Tables 5 to 8 below.

Table 5. Concentrations of TV ATCC 30001 Tested in Vaginal Swabs

Reagent Lot	Cells/mL	Positives/20 Replicates	Mean Ct		
			TV	SAC ^a	SPC ^b
Reagent Lot 1	0	0	0	21.5	33.8
	0.5	11	40.2	21.5	34.1
	1	12 ^c	40.0	21.4	34.0
	2	18	38.4	21.4	34.0
	3	20	38.5	21.5	34.0
	4	20	37.7	21.4	33.9
	6	20	37.1	21.4	33.9
Reagent Lot 2	0	0	0	22.1	34.0
	0.5	15	39.6	22.2	34.0
	1	18	40.0	22.1	33.8
	2	18	39.0	22.1	33.9
	3	20	38.3	22.1	34.0
	4	20	38.5	22.1	34.0

a. SAC (Sample Adequacy Control).

b. SPC (Sample Processing Control).

c. 1 of 20 replicates was reported as “ERROR”. The run was repeated resulting in a valid positive TV result.

Table 6. Concentrations of TV ATCC 30001 Tested in Vaginal Swabs

Reagent Lot	Cells/mL	Positives/20 Replicates	Mean Ct		
			TV	SAC	SPC
Reagent Lot 1	0	0	0	21.5	33.8
	0.5	9	40.0	21.6	34.2
	1	18	38.8	21.3	33.9
	2	18	38.4	21.5	33.9
	3	20	37.2	21.4	33.9
	4	20	37.0	21.5	33.9
	6	20	36.9	21.6	34.2
Reagent Lot 2	0	0	0	22.1	34.0
	0.5	13 ^a	40.0	22.0	34.0
	1	18	39.3	22.1	33.9
	2	18	38.1	22.2	34.0
	3	19	37.7	22.1	34.0
	4	20	37.3	22.0	34.0

a. 1 of 20 replicates was reported as “ERROR”. The run was repeated resulting in a valid positive TV result.

Table 7. Concentrations of TV ATCC 30001 Tested in Urine

Reagent Lot	Cells/mL	Positives/20 Replicates	Mean Ct		
			TV	SAC	SPC
Reagent Lot 1	0	0	0	29.1	33.8
	0.5	9 ^a	39.9	29.2	33.8
	1	18	39.1	29.2	33.8
	2	18	39.2	29.3	34.0
	3	19	38.1	29.3	34.1
	4	20	38.2	29.3	34.2
	6	20	37.2	29.2	33.9
Reagent Lot 2	0	0	0	30.1	34.0
	0.5	5	39.7	30.0	34.0
	1	16	39.5	30.1	34.0
	2	14	39.1	30.1	33.9
	3	20	39.1	30.1	34.2
	4	20	38.5	30.1	34.0

a. 2 of 20 replicates were reported as "ERROR". The runs were repeated resulting in valid positive TV results.

Table 8. Concentrations of TV ATCC 30001 Tested in Vaginal Swabs

Reagent Lot	Cells/mL	Positives/20 Replicates	Mean Ct		
			TV	SAC	SPC
Reagent Lot 1	0	0	0	29.1	33.8
	0.5	11	39.7	29.2	34.0
	1	11	39.2	29.3	33.9
	2	18	38.4	29.2	33.9
	3	20	37.8	29.3	34.0
	4	20	37.2	29.4	34.2
	6	20	37.5	29.3	34.0
Reagent Lot 2	0	0	0	30.1	34.0
	0.5	13	39.7	30.1	33.9
	1	17	39.3	30.1	34.0
	2	18	38.4	30.1	34.0
	3	20	38.6	30.1	34.0
	4	20	37.2	30.1	33.9

For each TV strain, the LoD estimate selected for verification was the highest value determined from the two lots. Verification of the estimated LoD claim was performed on one reagent lot across three testing days using 20 replicates per strain. The LoD was determined empirically as the lowest concentration that had 20/20 positive results. In addition to the empirical determination of LoD, Cepheid also conducted Probit analyses and the results were identical. One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells in

Cepheid Swab Transport Reagent, respectively). The data for this study was collected with the GenXpert Dx (GX-IV and GX-XVI) and the GeneXpert Infinity-80 Instruments. The LoD point values for each strain tested are summarized in Table 9 below.

Table.9 LoD of Two TV Strains in Either Pooled Vaginal Swab or Urine Matrix

<i>Trichomonas vaginalis</i> 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

The results of the LoD verification study indicate that the LoD for TV strains ATCC 30001 and ATCC 30238 in vaginal swab matrix is 2 cells/mL and that the LoD for TV strain ATCC 30001 in urine matrix is 3 cells/mL. The claimed LoD for TV strain ATCC 30238 in urine matrix is 2 cells/mL.

e. Analytical specificity:

Inclusivity

An inclusivity study was conducted to test reactivity of the Xpert TV Assay with 17 strains of TV, tested at a concentration of 3X LoD. The TV isolates were obtained from ATCC. TV cells were diluted into negative clinical matrix (either pooled vaginal swabs or urine in their respective Cepheid transport reagent). One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). The data for this study was collected with the GenXpert Infinity-80 Instrument. Results are summarized in Table 10.

Table 10. TV Strain Inclusivity for the 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

All 17 TV strains tested above were detected by the Xpert TV Assay.

Microbial Interference (Cross-Reactivity and Competitive Interference)

This study was conducted to evaluate interference in the Xpert TV Assay when non-target organisms are present at high concentrations. A panel of 124 microorganisms (5 viruses, 6 yeasts, 6 protozoans, and 107 bacteria) representing pathogens or flora commonly present in the urogenital system were evaluated. Each bacterial or fungal strain was tested at 1×10^6 CFU/mL or greater or at 1×10^6 genomes/mL. Viral strains were tested at 1×10^5 U/mL or 10^5 genomes/mL or greater. Protozoans were cultured in growth media, visually enumerated by light microscopy and tested at 1×10^5 cells/mL or greater or 10^5 genomes/mL. All microorganisms were tested in triplicate in the presence (competitive interference) and absence (cross-reactivity) of TV (ATCC 3001) at 3X LoD. All microorganisms tested were diluted into negative clinical matrix (either pooled vaginal swabs or urine in their respective Cepheid transport reagent).

One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). The data for this study was collected with the GenXpert Dx (GX-IV) Instrument.

One organism, *Trichomonas tenax*, demonstrated cross-reactivity (result of TV DETECTED in the absence of TV) at 1×10^5 cells/mL for the urine and vaginal swab matrix samples. This microorganism was subjected to repeat analysis at various other concentrations until a result of TV NOT DETECTED was obtained (at 1×10^2 cells/mL). 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 microbes. Results are summarized in Tables 11 and 12 for urine and vaginal swab matrix, respectively.

Table 11. Microbial Interference in Pooled Urine

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

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

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

Microorganism	Concentration Tested ^a	Xpert TV Assay Result	
		Cross-Reactivity (- <i>T. vaginalis</i>)	Competitive Interference (+ <i>T. vaginalis</i>)
<i>Proteus mirabilis</i>	1 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Proteus vulgaris</i>	1 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Providencia stuartii</i>	1 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Pseudomonas aeruginosa</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Pseudomonas fluorescens</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Pseudomonas putida</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Rahnella aquatilis</i>	1 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Rhodospirillum rubrum</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED
<i>Saccharomyces cerevisiae</i> ^e	6 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Salmonella minnesota</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Salmonella typhimurium</i>	1 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Serratia marcescens</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Staphylococcus aureus</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Staphylococcus epidermidis</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Staphylococcus saprophyticus</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus agalactiae</i>	1 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Streptococcus bovis</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus mitis</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus mutans</i>	2 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Streptococcus pneumoniae</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus pyogenes</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus salivarius</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus sanguis</i>	5 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptomyces griseinus</i>	6 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Trichomonas tenax</i> ^c	1 x 10 ⁵	TV DETECTED	TV DETECTED
<i>Trichomonas tenax</i> ^c	1 x 10 ³	TV DETECTED	TV DETECTED
<i>Trichomonas tenax</i> ^c	1 x 10 ²	TV NOT DETECTED	TV DETECTED
<i>Ureaplasma parvum</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED
<i>Ureaplasma urealyticum</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Vibrio parahaemolyticus</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Yersinia enterocolitica</i>	8 x 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, $\geq 10^5$ U/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 12. Microbial Interference in Vaginal Swab Matrix

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

Microorganism	Concentration Tested ^a	Xpert TV Assay Result	
		Cross-Reactivity (- <i>T. vaginalis</i>)	Competitive Interference (+ <i>T. vaginalis</i>)
<i>Corynebacterium genitalium</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Corynebacterium xerosis</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Cryptococcus neoformans</i> ^e	5 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Cryptosporidium parvum</i> ^c	1 x 10 ^{5d}	TV NOT DETECTED	TV DETECTED
Cytomegalovirus ^f	5 x 10 ⁵	TV NOT DETECTED	TV DETECTED
<i>Deinococcus radiodurans</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Derxia gummosa</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED
<i>Eikenella corrodens</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Entamoeba histolytica</i> ^c	1 x 10 ^{5d}	TV NOT DETECTED	TV DETECTED
<i>Enterobacter aerogenes</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Enterobacter cloacae</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Enterococcus avium</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Enterococcus faecalis</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Enterococcus faecium</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Erysipelothrix rhusiopathiae</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Escherichia coli</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Flavobacterium meningosepticum</i>	5 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Fusobacterium nucleatum</i> ^b	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Gardnerella vaginalis</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Gemella haemolysans</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Giardia intestinalis</i> ^c	1 x 10 ^{5d}	TV NOT DETECTED	TV DETECTED
<i>Haemophilus ducreyi</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED
<i>Haemophilus influenzae</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
Herpes simplex virus I ^f	1 x 10 ⁵	TV NOT DETECTED	TV DETECTED
Herpes simplex virus II ^f	1 x 10 ⁵	TV NOT DETECTED	TV DETECTED
HIV-1 ^f	2 x 10 ⁵	TV NOT DETECTED	TV DETECTED
Human papilloma virus 16 ^f	6 x 10 ⁵	TV NOT DETECTED	TV DETECTED
<i>Kingella dentrificans</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Kingella kingae</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Klebsiella oxytoca</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Klebsiella pneumoniae</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Lactobacillus acidophilus</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED

Microorganism	Concentration Tested ^a	Xpert TV Assay Result	
		Cross-Reactivity (- <i>T. vaginalis</i>)	Competitive Interference (+ <i>T. vaginalis</i>)
<i>Lactobacillus brevis</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Lactobacillus crispatus</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Lactobacillus jensonii</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Lactobacillus lactis</i>	1 x 10 ⁷	TV NOT DETECTED	TV DETECTED
<i>Lactobacillus vaginalis</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Legionella pneumophila</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Leuconostoc paramensenteroides</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Listeria monocytogenes</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Micrococcus luteus</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Mobiluncus curtisii</i> ^b	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Moraxella lacunata</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Moraxella osloensis</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Morganella morganii</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Mycobacterium smegmatis</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Mycoplasma genitalium</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED
<i>Mycoplasma hominis</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED
<i>Neisseria cinerea</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria dentrificans</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria elongata</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria flava</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria flavescens</i>	8 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria gonorrhoeae</i>	6 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria lactamica</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria mucosa</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria perflava</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria polysaccharea</i>	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria sicca</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Neisseria subflava</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Pantoea agglomerans</i>	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Paracoccus denitrificans</i>	6 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Pentatrichomonis hominis</i> ^c	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Peptostreptococcus anaerobius</i> ^b	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED

Microorganism	Concentration Tested ^a	Xpert TV Assay Result	
		Cross-Reactivity (- <i>T. vaginalis</i>)	Competitive Interference (+ <i>T. vaginalis</i>)
<i>Peptostreptococcus productus</i> ^b	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Plesiomonas shigelloides</i>	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Prevotella bivia</i> ^b	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Propionibacterium acnes</i> ^b	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Proteus mirabilis</i>	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Proteus vulgaris</i>	7 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Providencia stuartii</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Pseudomonas aeruginosa</i>	4x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Pseudomonas fluorescens</i>	5 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Pseudomonas putida</i>	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Rahnella aquatilis</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Rhodospirillum rubrum</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED
<i>Saccharomyces cerevisiae</i> ^e	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Salmonella minnesota</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Salmonella typhimurium</i>	5 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Serratia marcescens</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Staphylococcus aureus</i>	9 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Staphylococcus epidermidis</i>	5 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Staphylococcus saprophyticus</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus agalactiae</i>	6 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus bovis</i>	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus mitis</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus mutans</i>	5 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus pneumoniae</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus pyogenes</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus salivarius</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptococcus sanguis</i>	2 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Streptomyces griseinus</i>	4 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Trichomonas tenax</i> ^c	1 x 10 ⁵	TV DETECTED	TV DETECTED
<i>Trichomonas tenax</i> ^c	1 x 10 ³	TV DETECTED	TV DETECTED
<i>Trichomonas tenax</i> ^c	1 x 10 ²	TV NOT DETECTED	TV DETECTED
<i>Ureaplasma parvum</i>	1 x 10 ^{6d}	TV NOT DETECTED	TV DETECTED

Microorganism	Concentration Tested ^a	Xpert TV Assay Result	
		Cross-Reactivity (- <i>T. vaginalis</i>)	Competitive Interference (+ <i>T. vaginalis</i>)
<i>Ureaplasma urealyticum</i>	1 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Vibrio parahaemolyticus</i>	3 x 10 ⁶	TV NOT DETECTED	TV DETECTED
<i>Yersinia enterocolitica</i>	3 x 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, $\geq 10^5$ U/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

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 13.

Table 13. *In silico* Analysis for Microbial Interference

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

Potentially Interfering Substances

An interfering substances study was carried out to examine if substances or conditions that may be present in urine or vaginal swab specimens could affect the performance of the Xpert TV Assay. The panel consisted of endogenous substances such as blood, mucin, and leukocytes, and medications (prescription and over-the-counter) that could be used to treat urogenital conditions. Eight replicates were tested for each interfering substance. All substances were tested in the presence (interference) and absence (cross-reactivity) of TV (ATCC 3001) at 3X LoD. Substances were diluted in negative clinical matrix (either pooled vaginal swabs or urine in their respective Cepheid transport reagent) as appropriate. One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). The data for this study was collected with the GeneXpert Dx (GX-IV and GX-XVI) Instrument.

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. This substance (blood) was subjected to repeat analysis at various other 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 or cross-reactivity with the results of the Xpert TV Assay for these microbes. Results are summarized in Tables 14 and 15 for urine and vaginal swab matrix, respectively.

Table 14. Potentially Interfering Substances in Urine Samples

Class/Substance	Active Ingredient	Concentration Tested
Blood	Blood	0.3% v/v, 1% 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
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 15. 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

Class/Substance	Active Ingredient	Concentration Tested
	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
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 the labeling Section 14, Limitations.

Carry-Over

The purpose of the carry-over study was to uncover the presence of contamination in negative specimens due to carry-over of TV during nucleic acid extraction and amplification in the GeneXpert cartridge. The study was conducted over six days (not necessarily consecutive) on two modules using the same GeneXpert Dx Instrument (GX-IV). Twenty high positive samples were tested per module and 21 negative samples were tested per module. Two modules were used in the study for a total of 40 positive samples and 42 negative samples tested in the study. Negative samples consisted of pooled vaginal swab specimens in Cepheid Swab Transport Reagent and high positive samples consisted of 1 X 10⁶ cells/mL of TV ATCC 3001 in vaginal swab in Cepheid Swab Transport Reagent. High positive samples were alternated with negative samples. One TV positive and one negative control were tested daily (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively). All 42 replicates of negative sample were reported as “TV NOT DETECTED,” therefore, no evidence of carry-over was observed.

f. Assay cut-off:

Pre-clinical testing data generated with 309 prospectively collected clinical female samples (collected from 105 subjects, providing urine, endocervical swabs, and/or vaginal swab samples) was used to determine the valid minimum and maximum cycle threshold settings for TV. The results of this preliminary study indicated that the valid minimum cycle threshold setting for TV was 9 and the valid maximum cycle threshold setting for TV was 45.

These assay cut-offs were subsequently validated in the clinical study. For each specimen type, an analysis of receiver operator curves (ROCs) was conducted for the Xpert TV Assay results versus patient infected status (PIS) to confirm that the correct cut-off was chosen to optimize both sensitivity and specificity. The Youden’s Index and the Area Under the Curve (AUC) were used to make the final decision because the cut-off that maximizes the Youden’s index will give the optimal results in terms of sensitivity and specificity and the AUC gives an indication of how well the assay performs. In this study, all AUC statistics were greater than or equal to 98% and the Youden Index value was the highest at the chosen cut-off of 45 Ct.

The minimum and maximum Ct values observed for TV in the clinical study were 12 and 43.7, respectively. These values were within the valid minimum and maximum cycle threshold ranges described above. Taken together with the ROC analysis, these results indicate that the cut-off values selected for detection of TV with the Xpert Assay are appropriate.

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparison was based on the results from the Cepheid Xpert TV Assay on the GeneXpert Instrument Systems compared to the patient infected status (PIS) obtained from an FDA cleared NAAT assay and TV culture for all female specimen types (endocervical swabs, patient-collected vaginal swabs, and urine). The testing description and data are listed below in the Clinical Studies section.

b. *Matrix comparison:*

N/A

3. Clinical studies:

a. *Clinical Sensitivity and Specificity*

Specimen collection was conducted at 17 geographically diverse locations in the United States. Sites included (but were not limited to) OB/GYN, sexually transmitted disease (STD), and family planning clinics. Testing was conducted at 11 locations that represented the intended use sites for the Xpert TV Assay. For sites performing the Xpert TV Assay, positive and negative external controls (inactivated TV ATCC 30001 and human A549 cells in Cepheid Swab Transport Reagent, respectively) were tested with the assay on each day of testing. One testing site used a GeneXpert Infinity-80 Instrument. All other testing sites used the GeneXpert Dx Instrument (IV or XVI).

For each specimen type, results of the Xpert TV Assay were compared to a patient infected status (PIS) algorithm comprised of an FDA cleared NAAT test and culture. A specimen was called positive for PIS if either of the reference test results were positive. A specimen was called negative for PIS if both of the reference test results were negative. Specimens were collected in the following order: urine, vaginal swabs (patient-collected first then clinician-collected second), and endocervical swabs. Samples collected and tested on the Xpert TV Assay included first-catch urine, patient-collected vaginal swabs (collected in a clinical setting), and endocervical swabs. Two clinician-collected vaginal swabs were collected and used for reference testing. Three endocervical swabs were collected (two for reference testing and one for testing with the Xpert TV Assay). Study subjects were instructed to collect first-catch urine which was used for reference testing and testing with the Xpert TV Assay. Urine was collected from study subjects who had not urinated at least one hour prior to specimen collection.

Study participants were included in the study if they could provide informed consent, were sexually active, and were ≥ 14 years of age. Subjects were excluded from the study if they had been previously enrolled, received antimicrobial treatment within the previous 21 days, or had a history of hysterectomy (partial or complete removal of the cervix). The mean age of eligible study participants was 33.5 years (Range = 18 to 78 years old). A total of 1867 eligible female subjects were enrolled in the study. Of the 5383 valid Xpert TV Assay results (1799 endocervical swabs, 1791 vaginal swabs, and 1793 urine), 85 had initial ERROR, INVALID, or NO RESULT outcomes (1.58%; 95% CI 1.26-1.95). Upon retest, 77 of these specimens had valid results that were included in the final dataset used for the analyses and eight specimens had indeterminate results. These 8 specimens with indeterminate results were otherwise eligible specimens so were included in the calculation of indeterminate rate/assay success rate. The overall valid reporting rate for the assay was 99.9% (5383/5391). Specimens with discrepant results between the Xpert TV Assay and the PIS were analyzed by validated bi-directional Sanger sequencing and results are footnoted in Table 6 for informational purposes only.

For all three specimen types, there were no statistically significant differences between symptomatic and asymptomatic women for the performance of the Xpert TV Assay. Results from the clinical study are provided in Table 16.

Table 16. Clinical Study Results (Xpert TV Assay Results vs. PIS)

Sample Type	Status	Total (n)	Sens	95% CI	Spec	95% CI	Prev (%)	PPV (%)	NPV (%)
ES	Symp	685	100% (71/71)	94.9%-100%	98.5% (605/614)	97.2%-99.3%	10.4%	88.8%	100%
	Asymp	1114	98.1% (104/106)	93.4%-99.8%	99.1% (999/1008)	98.3%-99.6%	9.5%	92.0%	99.8%
	Overall	1799	98.9% (175/177) ^a	96.0%-99.9%	98.9% (1604/1622) ^b	98.3%-99.3%	9.8%	90.7%	99.9%
PC-VS	Symp	682	98.6% (73/74)	92.7%-100%	99.5% (605/608)	98.6%-99.9%	10.9%	96.1%	99.8%
	Asymp	1109	95.0% (113/119)	89.3%-98.1%	99.6% (986/990)	99.0%-99.9%	10.7%	96.6%	99.4%
	Overall	1791	96.4% (186/193) ^c	92.7%-98.5%	99.6% (1591/1598) ^d	99.1%-99.8%	10.8%	96.4%	99.6%
UR	Symp	688	98.6% (71/72)	92.5%-100%	99.8% (615/616)	99.1%-100%	10.5%	98.6%	99.8%
	Asymp	1105	98.2% (109/111)	93.6%-99.8%	99.6% (990/994)	99.0%-99.9%	10.0%	96.5%	99.8%
	Overall	1793	98.4% (180/183) ^e	95.3%-99.7%	99.7% (1605/1610) ^f	99.3%-99.9%	10.2%	97.3%	99.8%

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

- a. Testing results by sequencing: 1 of 2 FN was TV positive; 1 of 2 was TV negative.
- b. Testing results by sequencing: 8 of 18 FP were TV positive; 10 of 18 were TV negative.
- c. Testing results by sequencing: 3 of 7 FN were TV positive; 4 of 7 were TV negative.
- d. Testing results by sequencing: 5 of 7 FP were TV positive; 2 of 7 were TV negative.
- e. Testing results by sequencing: 3 of 3 FN were TV negative.
- f. Testing results by sequencing: 5 of 5 FP were TV negative.

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

During the clinical evaluation of the Xpert TV Assay, the observed prevalence of TV infection in females was 10.3%. 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 17. 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 16). The overall sensitivity and specificity for female urine (UR) were 98.4% and 99.7%, respectively. In patient-collected vaginal swab specimens (PC-VS), the overall sensitivity and specificity were 96.4% and 99.6%, respectively. For endocervical swabs (ES), the overall sensitivity and specificity were 98.9% and 98.9%, respectively.

Table 17. Hypothetical PPV and NPV of the Xpert TV Assay by Specimen Type

Specimen Type	Prevalence (%)	PPV (%)	NPV (%)
Female UR	1	76.2%	100.0%
	2	86.6%	100.0%
	5	94.3%	99.9%
	10	97.2%	99.8%
	12	97.7%	99.8%
	15	98.2%	99.7%
	20	98.8%	99.6%
	25	99.1%	99.5%
PC-VS	1	69.0%	100.0%
	2	81.8%	99.9%
	5	92.1%	99.8%
	10	96.1%	99.6%
	12	96.8%	99.5%
	15	97.5%	99.4%
	20	98.2%	99.1%
	25	98.7%	98.8%
ES	1	47.4%	100.0%
	2	64.5%	100.0%
	5	82.4%	99.9%
	10	90.8%	99.9%
	12	92.4%	99.8%
	15	94.0%	99.8%
	20	95.7%	99.7%
	25	96.7%	99.6%

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.