Roche Molecular Systems, Inc.
Nobuko Nakajima
Director, Regulatory Affairs
4300 Hacienda Drive
Pleasanton, California 94588-2722

May 22, 2019

Re: K190433
Trade/Device Name: cobas TV/MG for use on cobas 6800/8800 systems, cobas TV/MG Positive Control Kit, cobas Buffer Negative Control Kit
Regulation Number: 21 CFR 866.3393
Regulation Name: Device to Detect Nucleic Acids from Non-Viral Microorganism(s) Causing Sexually Transmitted Infections and Associated Resistance Marker(s)
Regulatory Class: Class II
Product Code: QEP
Dated: February 21, 2019
Received: February 22, 2019

Dear Nobuko Nakajima:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for

Uwe Scherf, Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K190433

Device Name
cobas TV/MG for use on cobas 6800/8800 systems, cobas TV/MG Positive Control Kit, cobas Buffer Negative Control Kit

Indications for Use *(Describe)*
cobas TV/MG on the cobas 6800/8800 Systems is an automated, qualitative in vitro nucleic acid diagnostic test that utilizes real-time polymerase chain reaction (PCR), for the direct detection of Trichomonas vaginalis (TV) and Mycoplasma genitalium (MG) DNA in male or female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical specimens, all collected in cobas PCR Media (Roche Molecular Systems, Inc.). cobas TV/MG also detects TV DNA in cervical specimens collected in PreservCyt solution and MG DNA in self-collected meatal swab specimens (collected in a clinical setting) and clinician-collected meatal swab specimens. This test is intended as an aid in the diagnosis of TV and MG infections in individuals suspected to have TV or MG infection.

A vaginal swab (self-collected or clinician-collected) is the preferred specimen type for MG testing in females due to higher sensitivity compared to endocervical swabs and urine. For males, urine is the preferred specimen type due to higher sensitivity compared to meatal swabs. If vaginal swab or male urine is not used and MG testing is negative, further testing with the preferred specimen type may be indicated if M. genitalium infection is strongly suspected.

Ancillary Collection Kits:

The cobas PCR Media Dual Swab Sample Kit is used to collect and transport human specimens. The cobas PCR Media serves as a nucleic acid stabilizing transport and storage medium for human specimens.
Note: This kit has been validated for use with the following tests:
• cobas CT/NG v2.0 Test (for use on the cobas 4800 Systems)
• cobas CT/NG for use on cobas 6800/8800 Systems
• cobas TV/MG for use on the cobas 6800/8800 Systems

The cobas PCR Media Uni Swab Sample Kit is used to collect and transport human specimens.
The cobas PCR Media serves as a nucleic acid stabilizing transport and storage medium for human specimens.
Note: This kit has been validated for use with the following tests:
• cobas CT/NG v2.0 Test (for use on the cobas 4800 Systems)
• cobas CT/NG for use on cobas 6800/8800 Systems
• cobas TV/MG for use on the cobas 6800/8800 Systems
• cobas Cdiff Test for use on the cobas 4800 System
• cobas Cdiff for use on the cobas Liat System

The cobas PCR Urine Sample Kit is used to collect and transport urine specimens. The cobas PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens.
Note: This kit has been validated for use with the following tests:
• cobas CT/NG v2.0 Test (for use on cobas 4800 Systems)
• cobas CT/NG for use on cobas 6800/8800 Systems
• cobas TV/MG for use on cobas 6800/8800 Systems

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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cobas® TV/MG
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Roche Molecular Systems, Inc.
Address	4300 Hacienda Drive Pleasanton, CA, 94588-2722
Contact	Nobuko Nakajima Phone: (925)730-8215 FAX: (925)225-0207 Email: nobuko.nakajima@roche.com
Date Prepared	February 21, 2019
Proprietary Name	**cobas**® TV/MG for use on **cobas**® 6800/8800 systems
Classification Name	21 CFR 866.3393 Nucleic acid detection system for non-viral microorganism(s) causing sexually transmitted infections 21 CFR 866.3860: Trichomonas vaginalis nucleic acid amplification test system
Product Codes	QEP: 21 CFR 866.3393 OUY: 21 CFR 866.3860
Predicate Devices	Aptima Mycoplasma genitalium assay (**DEN180047**)
Establishment Registration	Roche Molecular Systems, Inc. (2243471)

1. DEVICE DESCRIPTION

cobas® TV/MG on the **cobas**® 6800/8800 Systems is an automated, qualitative in vitro nucleic acid diagnostic test for the direct detection of *Trichomonas vaginalis* (TV) and *Mycoplasma genitalium* (MG) DNA in male or female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical specimens collected in **cobas**® PCR Media (Roche Molecular Systems, Inc.). **cobas**® TV/MG also detects TV DNA in cervical specimens collected in PreservCyt® Solution and MG DNA in self-collected meatal swab specimens (collected in a clinical setting) and clinician-collected meatal swab specimens. The DNA Internal Control, used to monitor the entire sample preparation and PCR

amplification process, is introduced into each specimen during sample processing. In addition, the test utilizes external controls (low titer positive control and a negative control).

1.1. Principles of the procedure

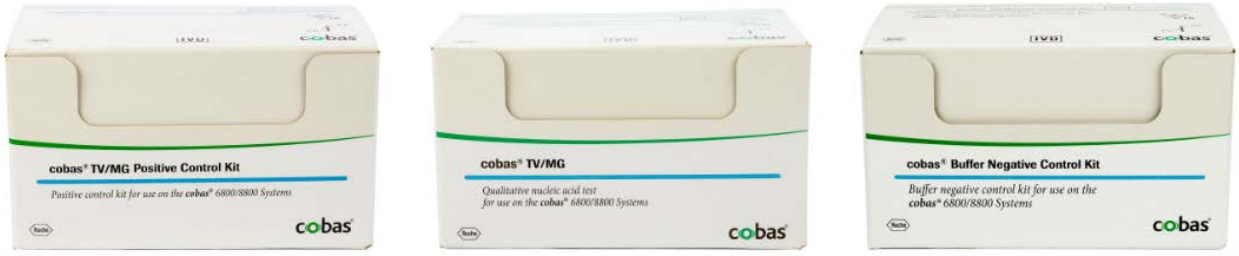
cobas® TV/MG is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. The **cobas**® 6800/8800 Systems consist of the sample supply module, the transfer module, the processing module, and the analytic module. Automated data management is performed by the **cobas**® 6800/8800 software which assigns test results for all tests as positive, negative or invalid. Results can be reviewed directly on the system screen, exported, or printed as a report.

Nucleic acid from patient samples and added internal control DNA (DNA-IC) molecules are simultaneously extracted. In summary, nucleic acid is released by addition of proteinase and lysis reagent to the sample. The released nucleic acid binds to the silica surface of the added magnetic glass particles. Unbound substances and impurities, such as denatured protein, cellular debris and potential PCR inhibitors are removed with subsequent wash steps and purified nucleic acid is eluted from the magnetic glass particles with elution buffer at elevated temperature. External controls (positive and negative) are processed in the same way with each **cobas**® TV/MG run.

Selective amplification of target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for TV and MG which are selected from highly-conserved regions within the respective target organism. TV is detected by one selective set of primers and a probe, while MG is detected by using two sets targeting separate regions (dual-target). Selective amplification of DNA IC is achieved by the use of sequence-specific forward and reverse primers which are selected to have no homology with either the TV or MG target regions. A thermostable DNA polymerase enzyme is used for PCR amplification. The target and DNA-IC sequences are amplified simultaneously utilizing a universal PCR amplification profile with predefined temperature steps and number of cycles. The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythymidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon). Any contaminating amplicon from previous PCR runs is eliminated by the AmpErase enzyme, which is included in the PCR master mix, during the first thermal cycling step. However, newly formed amplicons are not eliminated since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

The **cobas**® TV/MG master mix contains one detection probe specific for the TV target sequence, two detection probes specific for the MG target sequences and one for the DNA-IC. The probes are labeled with target specific fluorescent reporter dyes allowing simultaneous detection of TV target, MG targets and DNA-IC in three different target channels. When not bound to the target sequence, the fluorescent signal of the intact probes is suppressed by a quencher dye. During the PCR amplification step, hybridization of the probes to the specific single-stranded DNA template results in cleavage of the probe by the 5' to 3' exonuclease activity of the DNA polymerase resulting in separation of the reporter and quencher dyes and the generation of a fluorescent signal. With each PCR cycle, increasing amounts of cleaved probes are generated and the cumulative signal of the reporter dye increases concomitantly. Real-time detection and discrimination of PCR products is accomplished by measuring the fluorescence of the released reporter dyes for the TV and MG targets and DNA-IC, respectively.

Figure 1: cobas® TV/MG for use on the cobas® 6800/8800 Systems



2. INDICATIONS FOR USE

cobas TV/MG on the cobas 6800/8800 Systems is an automated, qualitative in vitro nucleic acid diagnostic test that utilizes real-time polymerase chain reaction (PCR), for the direct detection of *Trichomonas vaginalis* (TV) and *Mycoplasma genitalium* (MG) DNA in male or female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical specimens, all collected in cobas PCR Media (Roche Molecular Systems, Inc.). cobas TV/MG also detects TV DNA in cervical specimens collected in PreservCyt solution and MG DNA in self-collected meatal swab specimens (collected in a clinical setting) and clinician-collected meatal swab specimens. This test is intended as an aid in the diagnosis of TV and MG infections in individuals suspected to have TV or MG infection.

A vaginal swab (self-collected or clinician-collected) is the preferred specimen type for MG testing in females due to higher sensitivity compared to endocervical swabs and urine. For males, urine is the preferred specimen type due to higher sensitivity compared to meatal swabs. If vaginal swab or male urine is not used and MG testing is negative, further testing with the preferred specimen type may be indicated if *M. genitalium* infection is strongly suspected.

2.1. Ancillary Collection Kits

The **cobas**® PCR Media Dual Swab Sample Kit is used to collect and transport human specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for human specimens.

Note: This kit has been validated for use with the following tests:

- **cobas**® CT/NG v2.0 Test (for use on the **cobas**® 4800 Systems)
- **cobas**® CT/NG for use on **cobas**® 6800/8800 Systems
- **cobas**® TV/MG for use on the **cobas**® 6800/8800 Systems

The **cobas**® PCR Media Uni Swab Sample Kit is used to collect and transport human specimens.

The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for human specimens.

Note: This kit has been validated for use with the following tests:

- **cobas**® CT/NG v2.0 Test (for use on the **cobas**® 4800 Systems)
- **cobas**® CT/NG for use on **cobas**® 6800/8800 Systems
- **cobas**® TV/MG for use on the **cobas**® 6800/8800 Systems
- **cobas**® Cdiff Test for use on the **cobas**® 4800 System
- **cobas**® Cdiff for use on the cobas® Liat® System

The **cobas**® PCR Urine Sample Kit is used to collect and transport urine specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens.

Note: This kit has been validated for use with the following tests:

- **cobas**® CT/NG v2.0 Test (for use on **cobas**® 4800 Systems)
- **cobas**® CT/NG for use on **cobas**® 6800/8800 Systems

- **cobas**® TV/MG for use on **cobas**® 6800/8800 Systems

3. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the RMS **cobas**® TV/MG for use on the **cobas**® 6800/8800 systems are substantially equivalent to other legally marketed nucleic acid amplification tests intended for the qualitative detection of *Trichomonas vaginalis* (TV) and/or *Mycoplasma genitalium* (MG).

As indicated in Table 1, the **cobas**® TV/MNG for use on the **cobas**® 6800/8800 systems is substantially equivalent to significant characteristics of the identified predicate device, Hologic Aptima M. Genitalium Assay (DEN 180047).

Table 1: Comparison of the cobas® TV/MG for use on the cobas® 6800/8800 systems with the Predicate Devices

	Predicate Device: **Aptima Mycoplasma genitalium Assay (DEN180047)**	**Submitted Device** **cobas® TV/MG for use on the cobas® 6800/8800 systems**
Intended Use	The Aptima Mycoplasma genitalium assay is an in vitro nucleic acid amplification test (NAAT) for the qualitative detection of ribosomal RNA (rRNA) from Mycoplasma genitalium on the fully automated Panther® system. It is intended for use as an aid in the diagnosis of M. genitalium urogenital infections in male and female patients suspected of M. genitalium infection. The assay may be used to test the following specimens: clinician-collected and self-collected vaginal swabs (in a clinical setting), clinician-collected endocervical swabs, female and male urine, clinician-collected male urethral swabs, and self-collected penile meatal swabs (in a clinical setting). For females, a vaginal swab is the preferred specimen type due to higher clinical sensitivity for detecting M. genitalium than other specimen types; however, female urine or clinician-collected endocervical swabs may be used as alternative specimens when vaginal swab specimens are not available. If female urine or clinician-collected endocervical swab specimens test negative, testing with a vaginal swab may be	cobas TV/MG on the cobas 6800/8800 Systems is an automated, qualitative in vitro nucleic acid diagnostic test that utilizes real-time polymerase chain reaction (PCR), for the direct detection of *Trichomonas vaginalis* (TV) and *Mycoplasma genitalium* (MG) DNA in male or female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical specimens, all collected in cobas PCR Media (Roche Molecular Systems, Inc.). cobas TV/MG also detects TV DNA in cervical specimens collected in PreservCyt solution and MG DNA in self-collected meatal swab specimens (collected in a clinical setting) and clinician-collected meatal swab specimens. This test is intended as an aid in the diagnosis of TV and MG infections in individuals suspected to have TV or MG infection. A vaginal swab (self-collected or clinician-collected) is the preferred specimen type for MG testing in females due to higher sensitivity compared to endocervical swabs and urine. For males, urine is the preferred specimen type due to higher sensitivity compared to meatal swabs. If vaginal swab or male urine is

	Predicate Device: **Aptima Mycoplasma genitalium Assay (DEN180047)**	**Submitted Device** **cobas® TV/MG for use on the cobas® 6800/8800 systems**
	indicated, if M. genitalium infection is suspected.	not used and MG testing is negative, further testing with the preferred specimen type may be indicated if *M. genitalium* infection is strongly suspected.
Sample Types	• Clinician-collected and self-collected vaginal swabs (in a clinical setting), • Clinician-collected endocervical swabs, • Female and male urine, • Clinician-collected male urethral swabs, and • Self-collected penile meatal swabs (in a clinical setting)	TV and MG: • Male and female urine, • Self-collected/clinician-collected vaginal swab specimens in **cobas®** PCR Media, • Endocervical swab specimens in **cobas®** PCR Media, TV only: • Cervical specimens in PreservCyt® solution MG only: • Self-collected and clinician-collected penile meatal swabs
Conditions for use	For prescription use	Same
Amplification Technology	Target Capture (TC), Transcription Mediated Amplification (TMA)	Real-time PCR
Detection Chemistry	Hybridization Protection Assay (HPA)	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)
Result Analysis	Final assay results are interpreted based on the analyte signal-to-cutoff (S/CO).	Based on PCR cycle threshold analysis
Analyzer	Assay performed on the PANTHER Instrument	**cobas®** 6800/8800 systems
Sample Preparation Procedure	Automated	Same

4. NON-CLINICAL PERFORMANCE EVALUATION

4.1. Analytical sensitivity (Limit of Detection)

The limit of detection of **cobas®** TV/MG was determined by analysis of serial dilutions of quantified cultures of two *T. vaginalis* (RP - metronidazole susceptible and CDC085 - metronidazole resistant) and two *M. genitalium* (MG37 and M30) strains. Panels of six to seven

concentration levels with 60-72 replicates per specimen type and strain plus a blank were tested over three unique lots of **cobas**® TV/MG test reagents, multiple runs, days, operators, and instruments. LoD for each specimen type is shown in Table 2 as the target concentration which can be detected in ≥ 95% of the replicates for all lots.

Table 2: Analytical sensitivity (Limit of Detection)

Specimen Types	*T. vaginalis*				*M. genitalium*			
	RP strain		CDC085 strain		MG37 strain		M30 strain	
	LoD (cells/mL)	Mean Ct Value	LoD (cells/mL)	Mean Ct Value	LoD (copies/mL)	Mean Ct Value	LoD (copies/mL)	Mean Ct Value
Endocervical Swab in **cobas**® PCR Media	0.2	36.3	0.2	35.6	2	35.3	2	36.5
Vaginal Swab in **cobas**® PCR Media	0.3	35.5	0.075	36.3	4	34.5	4	35.3
Urine in **cobas**® PCR Media	0.1	35.7	0.03	35.6	0.5	35.6	1	35.8
Meatal Swab in **cobas**® PCR Media	N/A	N/A	N/A	N/A	0.5	36.0	0.5	36.6
Cervical Samples collected into PreservCyt® Solution	0.1	36.8	0.05	36.6	N/A	N/A	N/A	N/A

*N/A = Not Applicable

4.2. Inclusivity

Inclusivity of **cobas®** TV/MG was evaluated by testing eight TV and five MG laboratory strains using one lot of reagents. Testing was performed using TV and MG cultures diluted into contrived negative matrix. Results are shown in Table 3 and Table 4 for TV and MG strains, respectively. Twenty-four replicates per dilution level were tested for each strain in each matrix.

Table 3: LoD verification TV strains

Strain	Swabs*		Urine Specimens				PreservCyt® Specimens	
	cells/mL	% Pos	cells /mL	% Pos			cells /mL	% Pos
C-1:NIH	0.24	100	0.07	100			0.11	100

Strain	Swabs*		Urine Specimens				PreservCyt® Specimens	
	cells/mL	% Pos	cells /mL	% Pos			cells /mL	% Pos
123414	0.24	100	0.07	100			0.11	100
129155-8	0.24	100	0.07	100			0.11	100
CDC337	0.24	100	0.07	100			0.11	100
NYH 209	0.24	100	0.07	100			0.11	100
PRA-98	0.24	100	0.07	100			0.11	100
801805	0.24	100	0.07	100			0.11	100
BACT-053LR01	0.24	100	0.07	100			0.11	100

* Contrived vaginal swab matrix was used to represent vaginal and endocervical swab specimens.

Table 4: LoD verification MG strains

Strain	Swabs*		Urine Specimens		Meatal Swab			
	copies/mL	% Pos	copies /mL	% Pos	copies /mL	% Pos		
SEA-1	5.0	100	0.8	95.8	0.5	100		
M2288	5.0	100	0.8	100	0.5	100		
M2300	5.0	100	0.8	100	0.5	83.3		
M2321	5.0	100	1.6	100	1.0	87.5		
M2341	5.0	100	0.8	95.8	0.5	95.8		

* Contrived vaginal swab matrix was used to represent vaginal and endocervical swab specimens.

4.3. Precision (within laboratory)

In-house precision was examined using a panel composed of TV and MG cultures diluted into pooled negative urine stabilized in **cobas**® PCR Media, as well as in contrived matrices representing vaginal and meatal swab specimens collected in **cobas**® PCR Media or in cervical specimens collected in PreservCyt® Solution.

The precision panel for each matrix was designed to include members without TV and/or MG as well as those with high negative, low and moderate concentrations of TV and MG, corresponding to ~0.3x, ~1x and ~3x LoD. Testing was performed using three lots of **cobas**® TV/MG reagents and two instruments over twelve days and with two runs per day for a total of twenty-four runs. Each run consisted of three replicates of each sample. Description of the precision panels and the observed positivity rates are shown in Table 5. All negative panel members tested negative throughout the study.

Table 5: Summary of within laboratory precision

Level	N Tested	N positive TV	N positive MG	Hit Rate		95% Confidence Interval			
						TV		MG	
				TV	MG	Lower Limit	Upper Limit	Lower Limit	Upper Limit
Swabs collected in **cobas**® PCR Media									
Negative	72	0	0	0.0%	0.0%	0.0%	5.0%	0.0%	5.0%
High Negative	72	48	61	66.7%	84.7%	54.6%	77.3%	74.3%	92.1%
Low	71	69	70	97.2%	98.6%	90.2%	99.7%	92.4%	100%
Moderate	72	72	72	100%	100%	95.0%	100%	95.0%	100%
Urine stabilized in **cobas**® PCR Media									
Negative	72	0	0	0.0%	0.0%	0.0%	5.0%	0.0%	5.0%
High Negative	72	44	53	61.1%	73.6%	48.9%	72.4%	61.9%	83.3%
Low	72	72	72	100%	100%	95.0%	100%	95.0%	100%
Moderate	72	72	72	100%	100%	95.0%	100%	95.0%	100%
Meatal Swab collected in **cobas**® PCR Media									
Negative	72	N/A	0	N/A	0.0%	N/A	N/A	0.0%	5.0%
High Negative	72	N/A	41	N/A	56.9%	N/A	N/A	44.7%	68.6%
Low	72	N/A	69	N/A	95.8%	N/A	N/A	88.3%	99.1%
Moderate	72	N/A	72	N/A	100%	N/A	N/A	95.0%	100%
Cervical specimens collected in PreservCyt® Solution									
Negative	72	0	N/A	0.0%	N/A	0.0%	5.0%	N/A	N/A
High Negative	72	39	N/A	54.2%	N/A	42.0%	66.0%	N/A	N/A
Low	72	69	N/A	95.8%	N/A	88.3%	99.1%	N/A	N/A
Moderate	72	72	N/A	100%	N/A	95.0%	100%	N/A	N/A

*N/A = Not Applicable

Analysis of standard deviation and percent coefficient of variation of the Ct values from valid tests performed on positive panel members (see Table 6 and Table 7) yielded overall CV (%) ranges from 1.5% to 2.8% for TV and from 1.2% to 4.9% for MG.

Table 6: Overall mean, standard deviations and coefficients of variation (%) for cycle threshold, TV positive panels

Level	Hit Rate	Mean Ct	Within run		Between run		Between day		Between instrument		Between lot		Total	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Swabs collected in **cobas**® PCR Media														
High Negative	66.7%	37.6	0.98	2.6	0.0	0.0	0.0	0.0	0.26	0.7	0.22	0.7	1.04	2.8
Low	97.2%	36.5	0.62	1.7	0.22	0.6	0.00	0.0	0.60	1.6	0.19	0.5	0.91	2.5
Moderate	100.0%	35.5	0.38	1.1	0.05	0.2	0.03	0.1	0.74	2.1	0.15	0.4	0.85	2.4
Urine stabilized in **cobas**® PCR Media														
High Negative	61.1%	37.7	0.86	2.3	0.00	0.0	0.25	0.7	0.00	0.0	0.10	0.3	0.90	2.4
Low	100.0%	36.7	0.62	1.7	0.31	0.8	0.18	0.5	0.11	0.3	0.16	0.4	0.74	2.0
Moderate	100.0%	35.6	0.36	1.0	0.09	0.3	0.14	0.4	0.33	0.9	0.11	0.3	0.53	1.5
Cervical specimens collected in PreservCyt® Solution														
High Negative	54.2%	37.6	0.65	1.7	0.30	0.8	0.29	0.8	0.42	1.1	0.00	0.0	0.87	2.3
Low	95.8%	36.7	0.69	1.9	0.28	0.8	0.00	0.0	0.50	1.4	0.06	0.2	0.90	2.4
Moderate	100.0%	35.6	0.64	1.8	0.15	0.4	0.00	0.0	0.64	1.8	0.00	0.0	0.92	2.6

Table 7: Overall mean, standard deviations and coefficients of variation (%) for cycle threshold, MG positive panels

Level	Hit Rate	Mean Ct	Within run		Between run		Between day		Between instrument		Between lot		Total	
			SD	CV%	SD	CV%	SD	CV %	SD	CV%	SD	CV%	SD	CV%
Swabs collected in **cobas**® PCR Media														
High Negative	84.7%	37.2	1.29	3.5	0.00	0.0	0.00	0.0	0.98	2.6	0.00	0.0	1.62	4.3
Low	98.6%	35.6	0.56	1.6	0.00	0.0	0.16	0.5	0.71	2.0	0.05	0.1	0.92	2.6
Moderate	100.0%	34.7	0.26	0.7	0.00	0.0	0.05	0.1	0.73	2.1	0.10	0.3	0.78	2.3
Urine stabilized in **cobas**® PCR Media														
High Negative	73.6%	37.9	1.19	3.2	0.00	0.0	0.00	0.0	0.00	0.0	0.32	0.8	1.24	3.3
Low	100.0%	36.3	0.66	1.8	0.21	0.6	0.00	0.0	0.25	0.7	0.20	0.6	0.76	2.1
Moderate	100.0%	35.2	0.25	0.7	0.18	0.5	0.00	0.0	0.28	0.8	0.09	0.3	0.42	1.2

Meatal Swab collected in **cobas**® PCR Media														
High Negative	56.9%	38.1	1.55	4.1	0.37	1.0	0.00	0.0	0.95	2.5	0.00	0.0	1.85	4.9
Low	95.8%	37.0	0.78	2.1	0.00	0.0	0.00	0.0	0.39	1.1	0.00	0.0	0.87	2.4
Moderate	100.0%	35.7	0.33	0.9	0.00	0.0	0.00	0.0	0.32	0.9	0.18	0.5	0.50	1.4

4.4. Analytical specificity/cross reactivity

A panel of 102 bacteria, fungi and viruses, including those commonly found in the male and female urogenital tract, were tested with **cobas**® TV/MG to assess analytical specificity. The organisms listed in Table 8 were spiked at concentrations of approximately 1 x 10^6 units/mL for bacteria and approximately 1 x 10^5 units/mL for viruses into pooled negative urine stabilized in **cobas**® PCR Media. Testing was performed with each potential interfering organism in absence and presence of TV and MG target (spiked at approximately 3x LoD). Three replicates were tested for each organism in absence of target and one in presence of target. None of the organisms tested interfered with the test performance by generating false positive results for either TV or MG targets. Detection of MG target was not affected by any of the organisms tested. *Trichomonas tenax* interfered with detection of TV target at concentration level of 1 x 10^6 CFU/mL, but did not interfere with detection of TV target when tested at concentration level of 1 x 10^4 CFU/mL. *Trichomonas tenax* is a commensal of the oral cavity.

Table 8: Microorganisms tested for analytical specificity/cross reactivity

Microorganism	Microorganism	Microorganism
Acholeplasma laidlawii	*Enterococcus avium*	*Mycoplasma faucium*
Acholeplasma oculi	*Enterococcus faecalis*	*Mycoplasma fermentans*
Achromobacter xerosis	*Enterococcus faecium*	*Mycoplasma hominis*
Acinetobacter lwoffii	*Erysipelothrix rhusiopathiae*	*Mycoplasma orale*
Actinomyces israelii	*Escherichia coli*	*Mycoplasma penetrans*
Aerococcus viridans	*Flavobacterium*	*Mycoplasma pirum*
Aeromonas hydrophila	*Fusobacterium nucleatum*	*Mycoplasma pneumoniae*
Alcaligenes faecalis	*Gardnerella vaginalis*	*Mycoplasma primatum*
Atopobium vaginae	*Gemella haemolysans*	*Mycoplasma salivarium*
Bacillus subtilis	*Giardia intestinalis*	*Mycoplasma spermatophilum***
Bacteroides fragilis	*Haemophilus ducreyi*	*Neisseria gonorrhoeae*
Bacteroides ureolyticus	Herpes Simplex Virus Type 1*	*Pentatrichomonas hominis*
Bifidobacterium adolescentis	Herpes Simplex Virus Type 2*	*Peptostreptococcus anaerobius*

Microorganism	Microorganism	Microorganism
Branhamella catarrhalis	*Mycoplasma hominis*	*Prevotella bivia*
Brevibacterium linens	Human Immunodeficiency Virus*	*Propionibacterium acnes*
Campylobacter jejuni	Human Papillomavirus type 16	*Proteus mirabilis*
Candida albicans	*Kingella denitrificans*	*Providencia stuartii*
Candida glabrata	*Klebsiella oxytoca*	*Pseudomonas aeruginosa*
Candida parapilosis	*Klebsiella pneumoniae*	*Rahnella aquatilis*
Candida tropicalis	*Lactobacillus acidophilus*	*Rhizobium radiobacter*
Chlamydia trachomatis	*Lactobacillus crispatus*	*Rhodospirillum rubrum*
Chromobacterium violaceum	*Lactobacillus jensenii*	*Saccharomyces cerevisiae*
Citrobacter braakii	*Lactobacillus vaginalis*	*Salmonella minnesota*
Clostrodium perfringens	*Leptotrichia buccalis*	*Serratia marcescens*
*Clostridioides difficile***	*Leuconostoc mesenteroides*	*Staphylococcus aureus*
Corynebacterium genitalium	*Leuconostoc paramensenteroides*	*Staphylococcus epidermidis*
Corynebacterium xerosis	*Listeria monocytogenes*	*Streptococcus agalactiae*
Cryptococcus neoformans	*Micrococcus luteus*	*Streptococcus pneumoniae*
Cytomegalovirus	*Mobiluncus curtisii*	*Streptococcus pyogenes*
Derxia gummosa	*Moraxella osloensis*	*Trichomonas tenax****
Dientamoeba fragilis	*Morexella catarrhalis*	*Ureaplasma urealyticum*****
Eikenella corrodens	*Morexella lacunata*	*Veillonella parvula*
Enterobacter aerogenes	*Morganella morganii*	*Vibrio parahaemolyticus*
Enterobacter cloacae	*Mycobacterium smegmatis*	*Yersinia enterocolitica*

Unless noted (below), bacteria and fungi were quantified as Colony Forming Units (CFU) and viruses were quantified as International Units (IU).
* Quantified in copies/mL
** Previously known as *Clostridium difficile*
***Interference with TV detection observed when tested at 1 x10^6 CFU/mL. No interference with TV detection observed when tested at 1 x 10^4 CFU/mL or below.
****Quantified in color changing units (ccu)

4.5. Interference

The effect of over-the-counter or prescription products that may be present in urogenital specimens (Table 9) were evaluated. Possible interference from glacial acetic acid occasionally utilized in cytologic evaluation of cervical specimens was also assessed. Testing was done using pooled negative clinical specimens in the presence of TV and MG (spiked at approximately 3x LoD), and non-clinical/contrived matrices when testing in the absence of TV and MG. For each specimen type, three replicates were tested for each substance in the presence of and one in the absence of target organisms.

Eighteen products (including glacial acetic acid) as listed in Table 9 did not interfere with **cobas**® TV/MG when tested at concentrations of 1.0mg/mL or 1% v/v as applicable.

Table 9: List of products that do not interfere with test performance in urogenital specimens

Product Name		
Clindamycin Phosphate Vaginal Cream	Monistat® Complete Care Itch Relief Cream	Yeast Guard Advanced
CVS tioconazole 1 (Equate tioconazole 1)	Gyne-Lotrimin 7	Glacial acetic acid
Equate Vagicaine Anti-Itch Cream	Norforms Suppositories	Azo Standard
Estrace	Premarin	Arilin rapid vaginal suppositories
K-Y™ UltraGel (Replaces KY Silk E)	Summer's Eve Feminine Deodorant Spray	Vagi Metro Cream
Monistat 3 Vaginal Antifungal Combination Pack	Vaginal Contraceptive Foam	Nidazea Gel

Only Replens™, RepHresh™ Clean Balance, and Metronidazole Vaginal Gel by Sandoz interfered with **cobas**® TV/MG by producing false negative or invalid results at the concentrations above those stated in Table 10. It should be noted that three other products containing metronidazole (Arilin rapid vaginal suppositories, Vagi Metro Cream and Nidazea Gel), did not cause interference (Table 9).

Table 10: List of products that interfere with test performance above the concentration stated

Product Name	Swabs*	Urine Specimens	Meatal Swab	PreservCyt® Specimens
	mg/mL	mg/mL	mg/mL	mg/mL
Replens™ Long-Lasting Vaginal Moisturizer	1.0	0.5	0.3	2.0
RepHresh™ Clean Balance	2.0	1.0	0.5	2.0
Metronidazole Vaginal Gel by Sandoz	1.0	0.2	0.3	1.0

* Vaginal swab samples were used as a representative swab sample type for vaginal and endocervical swab specimens.

Endogenous substances that may be present in urogenital specimens were tested for interference. Testing was done using pooled negative clinical specimens in the presence of TV and MG (spiked at approximately 3x LoD), and non-clinical/contrived matrices when testing in the absence of TV and MG. At least twelve replicates were tested in total for each substance per condition across specimen types where the endogenous substances are expected to be present.

None of the substances interfered with the test performance by generating false-negative or false-positive results. Levels of endogenous substances tolerated by the assay for all specimen types are shown in Table 11.

Table 11: Summary of endogenous substance concentrations that do not show interference

Interferent	Swabs**	Meatal Swab	PreservCyt® Specimens	Urine
Albumin (% w/v)	N/A	N/A	N/A	0.5%
Bilirubin (% w/v)	N/A	N/A	N/A	1.0%
Mucus*	present	present	present	present
Glucose (% w/v)	N/A	N/A	N/A	1.0 %
Peripheral Blood Mononuclear Cells	1.0E+06 cells/mL	N/A	1.0E+06 cells/mL	1.0E+06 cells/mL
pH (acidic and alkaline)	N/A	N/A	N/A	pH 4 and pH 9
Semen	22 mg/mL	20 mg/mL	4 mg/mL	13 mg/mL
Whole Blood (% v/v)	10%	N/A	10%	10%

* One mucus swab per sample reflecting the maximum level that could be found in patient sample.

**Endocervical swab samples were used as a representative swab sample type for vaginal and endocervical swab specimens.

***Semen tested from swab dipped in fluid. Swab was weighed before and after to determine concentration.

4.6. Competitive inhibition

To assess competitive inhibition between TV and MG, samples of swabs, urine and PreservCyt® specimens were tested with low and moderate concentrations of one target mixed with very high concentrations of the opposite target. Low and moderate concentrations were defined as ~1x LoD and ~3x LoD, respectively, and high concentrations ($\geq 10^5$ cells/mL for TV and $\geq 10^5$ copies/mL for MG) were defined as those generating a signal greater than observed in 95% of target positive clinical specimens.

Testing results indicated that when MG was present at a high concentration, TV was detected in all specimen types, at both the low (~1x LoD) and moderate (~3x LoD) levels. Results also indicated that when TV was present at a high concentration, MG was detected in all specimen types at both the low (~1x LoD) and moderate (~3x LoD) levels.

4.7. Cross contamination/Carryover

Studies were performed to evaluate potential cross-contamination on the **cobas**® 6800/8800 Systems using **cobas**® TV/MG. Cross-contamination can cause false positive results. In this performance study the sample-to-sample cross-contamination rate of **cobas**® TV/MG has been determined to be 0.7% (4/576, upper one-sided 95% CI of 1.6%) for TV and 0.0% (0/480, upper one-sided 95% CI of 0.6%) for MG when alternating very high positive and negative samples were tested over 11 runs for TV and 10 runs for MG. Run-to-run cross-contamination has not been observed (0/188). Testing was done using samples prepared with **cobas**® PCR Media and with PreservCyt® Solution. High positive samples in the study were prepared to generate a Ct value that exceeds 95% or more of signal obtained from specimens of infected patients in the intended use population. Cross contamination rates in clinical settings depend on the proportion of high positive samples and prevalence of the disease. Routine clinical cross-contamination rates need to be assessed in user setting.

5. CLINICAL PERFORMANCE EVALUATION

5.1. Reproducibility study

A reproducibility study was performed across different sites, lots, days, operators/batches, for **cobas**® TV/MG using panels prepared from vaginal swabs, meatal swabs, and urine in **cobas**® PCR Media and cervical specimens in PreservCyt® Solution. Testing was performed at two external sites and one site that was in-house at Roche Molecular Systems. One panel consisted of 4 sample matrices, with six concentrations per matrix, and three replicates per concentration for a total of 72-samples in one panel. A batch was comprised of one 72-sample panel and two controls (one positive and negative control). Two operators at each site tested one batch each per day. Two valid batches had to be completed within a 24-hour period. Each site received two of three reagent lots and performed 6 days of testing per reagent lot for a total of 12 days of testing.

5.1.1. Negative panels

For each sample type, the percent of correct results for all combined TV negative panel members (i.e., “Negative TV, Negative MG” and “Negative TV, ~1.0x LoD MG”) ranged from 99.3% to 100% (432/432). All of the valid tests from each of the urine and PreservCyt® sample types were negative and the percent of correct results was estimated at 100% (432/432) with a corresponding 95% Clopper–Pearson exact CI of (99.1%, 100%). For vaginal swab, the percent

of correct results was estimated as 99.3% (429/432) with a corresponding 95% Clopper–Pearson exact CI of (98.0%, 99.9%) for TV.

For each sample type, the percent of correct results for all combined MG negative panel members (i.e., "Negative TV, Negative MG" and "~1.0x LoD TV, Negative MG") ranged from 99.8% to 100%. All of the valid tests from each of the urine and vaginal swab sample types were negative and the percent of correct results was estimated at 100% (432/432) with a corresponding 95% Clopper–Pearson exact CI of (99.1%, 100%). For meatal swab, the percent of correct results for MG was estimated as 99.8% (431/432) with a corresponding 95% Clopper–Pearson exact CI of (98.7%, 100%).

5.1.2. *Trichomonas vaginalis* panels

For each positive panel member, precision was evaluated using a random effects model by sample type with terms for lot, site, day, operator/batch within site, lot and day, and within-batch components by the corresponding analyte cycle threshold (Ct) values of **cobas**® TV/MG. Table 12 presents the total SD, and total percent CV (%) from these analyses. The range of the total CV, across the positive panel members, was from 1.2% to 2.7%. The maximum total CV was observed in the PCR Media/Urine with the "~1.0x LoD TV, ~3.0x LoD MG" panel member and most of that variability (95.2% of the total variance) was explained by random error (within-batch).

Table 12: TV: mean estimate, attributable percentage of total variance, total precision standard deviation, and CV(%) of cobas® TV/MG cycle threshold (Ct) values by TV positive panel member for each specimen type

				Percentage of Total Variance [CV(%)]					Total Precision	
Specimen	Panel Member	N[a]	Mean Estimate[b]	Lot	Site	Day	Operator/ Batch	Within-Batch	SD[b]	CV(%)[c]
PCR Media/Urine	~0.3x LoD TV, ~0.3x LoD MG	121	38.1	0.0% (0.0)	6.5% (0.5)	0.0% (0.0)	17.6% (0.9)	75.9% (1.8)	0.79	2.1
	~1.0x LoD TV, Negative MG	216	36.7	10.3% (0.6)	3.6% (0.4)	2.3% (0.3)	3.6% (0.4)	80.3% (1.7)	0.69	1.9
	~3.0x LoD TV, ~1.0x LoD MG	216	35.7	10.6% (0.4)	2.4% (0.2)	3.0% (0.2)	2.9% (0.2)	81.1% (1.2)	0.48	1.3
	~1.0x LoD TV, ~3.0x LoD MG	214	36.4	0.0% (0.0)	0.9% (0.3)	0.0% (0.0)	3.9% (0.5)	95.2% (2.7)	0.99	2.7
PCR Media/ Vaginal Swab	~0.3x LoD TV, ~0.3x LoD MG	103	37.7	0.0% (0.0)	0.0% (0.0)	14.7% (0.8)	0.0% (0.0)	85.3% (1.9)	0.77	2.0

				Percentage of Total Variance [CV(%)]					Total Precision	
Specimen	**Panel Member**	**N[a]**	**Mean Estimate[b]**	**Lot**	**Site**	**Day**	**Operator/ Batch**	**Within-Batch**	**SD[b]**	**CV(%)[c]**
	~1.0xLoD TV, Negative MG	215	36.0	1.5% (0.2)	1.4% (0.2)	0.0% (0.0)	14.5% (0.6)	82.6% (1.5)	0.59	1.6
	~3.0x LoD TV, ~1.0x LoD MG	216	35.0	16.4% (0.5)	2.7% (0.2)	5.4% (0.3)	0.0% (0.0)	75.5% (1.0)	0.40	1.2
	~1.0x LoD TV, ~3.0x LoD MG	213	36.4	0.6% (0.2)	0.0% (0.0)	2.1% (0.3)	0.0% (0.0)	97.3% (2.3)	0.85	2.3
PreservCyt®/ Cervical	~0.3x LoD TV, ~0.3x LoD MG	79	37.7	0.0% (0.0)	0.4% (0.1)	0.0% (0.0)	0.0% (0.0)	99.6% (2.3)	0.86	2.3
	~1.0x LoD TV, Negative MG	190	37.2	0.0% (0.0)	1.3% (0.2)	0.0% (0.0)	7.0% (0.6)	91.7% (2.1)	0.81	2.2
	~3.0x LoD TV, ~1.0x LoD MG	215	35.5	3.5% (0.2)	5.8% (0.3)	0.8% (0.1)	0.6% (0.1)	89.3% (1.2)	0.45	1.3
	~1.0x LoD TV, ~3.0x LoD MG	210	36.7	0.6% (0.1)	3.9% (0.4)	0.0% (0.0)	0.0% (0.0)	95.5% (1.8)	0.67	1.8

Note: The table only includes results with detectable analyte.
CV(%) = Percent Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium;* SD = Standard Deviation; TV = *Trichomonas vaginalis*.
[a] Number of valid tests with a TV positive result that contributed a Ct value to the analysis. Because only TV positive test results were included, estimates of SD (and CV%) may be underestimated.
[b] Calculated using the total variability from the SAS MIXED procedure.
[c] CV(%) = (standard deviation / mean) × 100%.

The TV percent agreement and observed summary statistics are presented by lot, site, day and operator/batch in Table 13 to Table 15, respectively for **cobas**® PCR Media/urine, **cobas**® PCR Media/vaginal swab, and PreservCyt®/cervical sample types.

Table 13: TV percent agreement by panel member for lot, site, day and operator/batch - cobas® PCR Media/urine

PCR Media/Urine											
	Observed Descriptive Statistics[a]				TV Positive Percent Agreement[b]						
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~0.3x LoD TV, ~0.3x LoD MG	38.1	0.78	2.1	1	55.6% (40/72)	1	51.4% (37/72)	1	47.2% (17/36)	1	56.5% (61/108)
				2	55.6% (40/72)	2	58.3% (42/72)	2	52.8% (19/36)	2	55.6% (60/108)
				3	56.9% (41/72)	3	58.3% (42/72)	3	50.0% (18/36)		
								4	58.3% (21/36)		
								5	61.1% (22/36)		
								6	66.7% (24/36)		
~1.0x LoD TV, Negative MG	36.7	0.68	1.9	1	100% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		
~3.0x LoD TV, ~1.0x LoD MG	35.7	0.47	1.3	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

PCR Media/Urine											
	Observed Descriptive Statistics[a]			TV Positive Percent Agreement[b]							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~1.0x LoD TV, ~3.0x LoD MG	36.4	0.99	2.7	1	100.0% (72/72)	1	98.6% (71/72)	1	100.0% (36/36)	1	98.1% (106/108)
				2	98.6% (71/72)	2	98.6% (71/72)	2	97.2% (35/36)	2	100.0% (108/108)
				3	98.6% (71/72)	3	100.0% (72/72)	3	97.2% (35/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

Note: Ct = Cycle threshold; CV = Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium*; SD = Standard Deviation; TV = *Trichomonas vaginalis*.

Note: CV(%) = (standard deviation / mean) × 100%. Because only TV positive test results were included in the Ct descriptive statistics calculations, estimates of SD (and CV%) may be underestimated.

[a] Calculated using the SAS MEANS procedure.

[b] TV Positive Percent Agreement = (number of TV positive results / number of valid test results) × 100%.

Table 14: TV: Percent agreement by panel member for lot, site, day and operator/batch-cobas® PCR Media/vaginal swab

PCR Media/Vaginal Swab											
	Observed Descriptive Statistics[a]			TV Positive Percent Agreement[b]							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~0.3x LoD TV, ~0.3x LoD MG	37.7	0.77	2.0	1	48.6% (35/72)	1	40.3% (29/72)	1	52.8% (19/36)	1	43.5% (47/108)
				2	40.3% (29/72)	2	61.1% (44/72)	2	52.8% (19/36)	2	51.9% (56/108)
				3	54.2% (39/72)	3	41.7% (30/72)	3	38.9% (14/36)		
								4	50.0% (18/36)		
								5	36.1% (13/36)		
								6	55.6% (20/36)		
~1.0x LoD TV, Negative MG	36.0	0.59	1.6	1	98.6% (71/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	98.6% (71/72)	2	100.0% (36/36)	2	99.1% (107/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	97.2% (35/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		
~3.0x LoD TV, ~1.0x LoD MG	35.0	0.40	1.1	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

PCR Media/Vaginal Swab											
	Observed Descriptive Statistics[a]			TV Positive Percent Agreement[b]							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~1.0x LoD TV, ~3.0x LoD MG	36.4	0.85	2.3	1	97.2% (70/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	98.1% (106/108)
				2	98.6% (71/72)	2	97.2% (70/72)	2	94.4% (34/36)	2	99.1% (107/108)
				3	100.0% (72/72)	3	98.6% (71/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	97.2% (35/36)		

Note: Ct = Cycle threshold; CV = Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium*; SD = Standard Deviation; TV = *Trichomonas vaginalis*.

Note: CV(%) = (standard deviation / mean) × 100%. Because only TV positive test results were included in the Ct descriptive statistics calculations, estimates of SD (and CV%) may be underestimated.

[a] Calculated using the SAS MEANS procedure.

[b] TV Positive Percent Agreement = (number of TV positive results / number of valid test results) × 100%.

Table 15: TV: Percent agreement by panel member for lot, site, day and operator/batch-cobas® PCR Media/PreservCyt®

PreservCyt®/Cervical											
	Observed Descriptive Statistics[a]			TV Positive Percent Agreementb[a]							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~0.3x LoD TV, ~0.3x LoD MG	37.7	0.86	2.3	1	43.1% (31/72)	1	31.0% (22/71)	1	40.0% (14/35)	1	41.5% (44/106)
				2	33.3% (24/72)	2	36.6% (26/71)	2	52.8% (19/36)	2	32.4% (35/108)
				3	34.3% (24/70)	3	43.1% (31/72)	3	38.9% (14/36)		
								4	25.0% (9/36)		
								5	27.8% (10/36)		
								6	37.1% (13/35)		
~1.0x LoD TV, Negative MG	37.2	0.81	2.2	1	91.7% (66/72)	1	87.3% (62/71)	1	88.9% (32/36)	1	85.0% (91/107)
				2	88.7% (63/71)	2	87.5% (63/72)	2	77.8% (28/36)	2	91.7% (99/108)
				3	84.7% (61/72)	3	90.3% (65/72)	3	85.7% (30/35)		
								4	88.9% (32/36)		
								5	91.7% (33/36)		
								6	97.2% (35/36)		
~3.0x LoD TV, ~1.0x LoD MG	35.5	0.45	1.3	1	100.0% (72/72)	1	100.0% (71/71)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (71/71)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (107/107)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (35/35)		

PreservCyt®/Cervical											
	Observed Descriptive Statistics			TV Positive Percent Agreement[a]							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~1.0x LoD TV, ~3.0x LoD MG	36.7	0.67	1.8	1	98.6% (71/72)	1	97.2% (70/72)	1	100.0% (36/36)	1	99.1% (107/108)
				2	95.8% (69/72)	2	97.2% (70/72)	2	94.4% (34/36)	2	95.4% (103/108)
				3	97.2% (70/72)	3	97.2% (70/72)	3	94.4% (34/36)		
								4	97.2% (35/36)		
								5	97.2% (35/36)		
								6	100.0% (36/36)		

Note: Ct = Cycle threshold; CV = Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium*; SD = Standard Deviation; TV = *Trichomonas vaginalis*.
Note: CV(%) = (standard deviation / mean) × 100%. Because only TV positive test results were included in the Ct descriptive statistics calculations, estimates of SD (and CV%) may be underestimated.
a Calculated using the SAS MEANS procedure.[b] TV Positive Percent Agreement = (number of TV positive results / number of valid test results) × 100%.

5.1.3. *Mycoplasma genitalium* panels

For each positive panel member, precision was evaluated using a random effects model by sample type with terms for lot, site, day, operator/batch within site, lot and day, and within-batch components on the corresponding analyte cycle threshold (Ct) values of **cobas**® TV/MG. Table 16 presents the total SD and total CV (%) from these analyses. The range of the total coefficient of variation, among positive panel members, was from 0.8% to 4.0%. The higher total coefficient of variation was observed in the lowest concentration of positive panel members (~0.3x LoD TV, ~0.3x LoD MG) for all sample types and most of that variability (75.8% for PCR Media/urine, 100% for PCR Media/vaginal swab, and 83.7% for PCR Media/vaginal swab) was explained by random error (within-batch).

Table 16: MG: attributable percentage of total variance, total precision standard deviation, and CV(%) of cobas® TV/MG cycle threshold (Ct) values by MG positive panel member for each media type

				Percentage of Total Variance [CV(%)]					Total Precision	
Media Type	Panel Member	N[a]	Mean Estimate[b]	Lot	Site	Day	Operator/ Batch	Within-Batch	SD[b]	CV(%)[c]
PCR Media/Urine	~0.3x LoD TV, ~0.3x LoD MG	154	38.1	2.4% (0.4)	0.0% (0.0)	7.7% (0.7)	14.1% (1.0)	75.8% (2.3)	1.01	2.6
	Negative TV, ~1.0x LoD MG	216	36.5	10.2% (0.5)	0.0% (0.0)	0.0% (0.0)	5.7% (0.4)	84.1% (1.3)	0.54	1.5
	~3.0x LoD TV, ~1.0x LoD MG	214	36.3	3.9% (0.4)	2.8% (0.3)	9.4% (0.6)	0.0% (0.0)	83.9% (1.7)	0.69	1.9
	~1.0x LoD TV, ~3.0x LoD MG	216	29.7	7.7% (0.2)	15.3% (0.3)	10.2% (0.3)	20.1% (0.4)	46.7% (0.6)	0.26	0.9
PCR Media/ Vaginal Swab	~0.3x LoD TV, ~0.3x LoD MG	107	37.9	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	100.0% (4.0)	1.50	4.0
	Negative TV, ~1.0x LoD MG	214	35.7	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	100.0% (2.3)	0.84	2.3
	~3.0x LoD TV, ~1.0x LoD MG	216	35.2	4.7% (0.3)	2.6% (0.2)	0.0% (0.0)	0.4% (0.1)	92.3% (1.1)	0.42	1.2
	~1.0x LoD TV, ~3.0x LoD MG	216	34.4	5.6% (0.2)	17.2% (0.3)	0.0% (0.0)	0.0% (0.0)	77.2% (0.7)	0.29	0.8
PCR Media/ Meatal Swab	~0.3x LoD TV, ~0.3x LoD MG	115	38.2	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	16.3% (1.1)	83.7% (2.6)	1.09	2.8
	Negative TV, ~1.0x LoD MG	216	35.9	11.7% (0.4)	5.3% (0.3)	7.6% (0.3)	0.0% (0.0)	75.4% (1.0)	0.42	1.2
	~3.0x LoD TV, ~1.0x LoD MG	215	36.7	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	100.0% (2.2)	0.81	2.2
	~1.0x LoD TV, ~3.0x LoD MG	216	35.8	16.3% (0.4)	1.0% (0.1)	0.0% (0.0)	2.0% (0.2)	80.7% (1.0)	0.40	1.1

Note: The table only includes results with detectable analyte.
CV(%) = Percent Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium;* SD = Standard Deviation; TV = *Trichomonas vaginalis.*
[a] Number of valid tests with a MG positive result that contributed a Ct value to the analysis. Because only MG positive test results were included, estimates of SD (and CV%) may be underestimated.
[b] Calculated using the total variability from the SAS MIXED procedure.
[c] CV(%) = (standard deviation / mean) × 100%.

The MG positive percent agreement and observed summary statistics (mean, SD, CV (%),cycle threshold (Ct) value for MG target) are presented by lot, site, day and operator/batch in Table 17 to Table 19, respectively for **cobas**® PCR Media/urine, **cobas**® PCR Media/vaginal swab, and **cobas**® PCR Media/meatal swab.

Table 17: MG: Percent agreement by panel member for lot, site, day and operator/batch-cobas® PCR Media/urine

PCR Media/Urine											
	Observed Descriptive Statistics[a]			MG Positive Percent Agreement							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~0.3x LoD TV, ~0.3x LoD MG	38.1	1.01	2.6	1	75.0% (54/72)	1	70.8% (51/72)	1	63.9% (23/36)	1	74.1% (80/108)
				2	68.1% (49/72)	2	75.0% (54/72)	2	83.3% (30/36)	2	68.5% (74/108)
				3	70.8% (51/72)	3	68.1% (49/72)	3	80.6% (29/36)		
								4	72.2% (26/36)		
								5	63.9% (23/36)		
								6	63.9% (23/36)		
Negative TV, ~1.0x LoD MG	36.5	0.53	1.4	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		
~3.0x LoD TV, ~1.0x LoD MG	36.3	0.68	1.9	1	98.6% (71/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	99.1% (107/108)
				2	100.0% (72/72)	2	97.2% (70/72)	2	100.0% (36/36)	2	99.1% (107/108)
				3	98.6% (71/72)	3	100.0% (72/72)	3	97.2% (35/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	97.2% (35/36)		

PCR Media/Urine											
	Observed Descriptive Statistics[a]			MG Positive Percent Agreement							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~1.0x LoD TV, ~3.0x LoD MG	29.7	0.26	0.9	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

Note: Ct = Cycle threshold; CV = Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium;* SD = Standard Deviation; TV = *Trichomonas vaginalis*.
Note: CV(%) = (standard deviation / mean) × 100%. Because only MG positive test results were included in the Ct descriptive statistics calculations, estimates of SD (and CV%) may be underestimated.
a Calculated using the SAS MEANS procedure.
[b] MG Positive Percent Agreement = (number of MG positive results / number of valid test results) × 100%.

Table 18: MG: Percent agreement by panel member for lot, site, day and operator/batch-cobas® PCR Media/vaginal swab

PCR Media/Vaginal Swab											
	Observed Descriptive Statistics[a]			MG Positive Percent Agreement							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~0.3x LoD TV, ~0.3x LoD MG	37.9	1.50	4.0	1	37.5% (27/72)	1	58.3% (42/72)	1	44.4% (16/36)	1	50.0% (54/108)
				2	56.9% (41/72)	2	51.4% (37/72)	2	63.9% (23/36)	2	49.1% (53/108)
				3	54.2% (39/72)	3	38.9% (28/72)	3	38.9% (14/36)		
								4	52.8% (19/36)		
								5	52.8% (19/36)		
								6	44.4% (16/36)		
Negative TV, ~1.0x LoD MG	35.7	0.84	2.3	1	97.2% (70/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	98.1% (106/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	97.2% (70/72)	3	100.0% (36/36)		
								4	97.2% (35/36)		
								5	100.0% (36/36)		
								6	97.2% (35/36)		
~3.0x LoD TV, ~1.0x LoD MG	35.2	0.42	1.2	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

PCR Media/Vaginal Swab											
	Observed Descriptive Statistics[a]			MG Positive Percent Agreement							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~1.0x LoD TV, ~3.0x LoD MG	34.4	0.29	0.8	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

Note: Ct = Cycle threshold; CV = Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium*; SD = Standard Deviation; TV = *Trichomonas vaginalis*.
Note: CV(%) = (standard deviation / mean) × 100%. Because only MG positive test results were included in the Ct descriptive statistics calculations, estimates of SD (and CV%) may be underestimated.
a Calculated using the SAS MEANS procedure.
[a] MG Positive Percent Agreement = (number of MG positive results / number of valid test results) × 100%.

Table 19: MG: Percent agreement by panel member for lot, site and day - cobas® PCR Media/meatal swab

PCR Media/Meatal Swab											
	Observed Descriptive Statistics			MG Positive Percent Agreement[a]							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~0.3x LoD TV, ~0.3x LoD MG	38.2	1.09	2.8	1	48.6% (35/72)	1	52.9% (37/70)	1	69.4% (25/36)	1	60.4% (64/106)
				2	59.7% (43/72)	2	55.6% (40/72)	2	50.0% (18/36)	2	47.2% (51/108)
				3	52.9% (37/70)	3	52.8% (38/72)	3	38.9% (14/36)		
								4	52.8% (19/36)		
								5	57.1% (20/35)		
								6	54.3% (19/35)		
Negative TV, ~1.0x LoD MG	35.9	0.41	1.2	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		
~3.0x LoD TV, ~1.0x LoD MG	36.7	0.81	2.2	1	100.0% (72/72)	1	98.6% (71/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	99.1% (107/108)
				3	98.6% (71/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	97.2% (35/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

PCR Media/Meatal Swab											
	Observed Descriptive Statistics			MG Positive Percent Agreement[a]							
Panel Member	Ct Mean	Ct SD	Ct CV(%)		Lot		Site		Day		Operator/ Batch
~1.0x LoD TV, ~3.0x LoD MG	35.8	0.39	1.1	1	100.0% (72/72)	1	100.0% (72/72)	1	100.0% (36/36)	1	100.0% (108/108)
				2	100.0% (72/72)	2	100.0% (72/72)	2	100.0% (36/36)	2	100.0% (108/108)
				3	100.0% (72/72)	3	100.0% (72/72)	3	100.0% (36/36)		
								4	100.0% (36/36)		
								5	100.0% (36/36)		
								6	100.0% (36/36)		

Note: Ct = Cycle threshold; CV = Coefficient of Variation; LoD = Limit of Detection; MG = *Mycoplasma genitalium*; SD = Standard Deviation; TV = *Trichomonas vaginalis*.
Note: CV(%) = (standard deviation / mean) × 100%. Because only MG positive test results were included in the Ct descriptive statistics calculations, estimates of SD (and CV%) may be underestimated.
a Calculated using the SAS MEANS procedure
[a] MG Positive Percent Agreement = (number of MG positive results / number of valid test results) × 100%.

5.1.4. Percentage agreement

Table 20 shows the percent agreement for each target (TV and MG) with the associated 95% Exact CI.

Table 20: Percent agreement for panel members with concentration at or near 1x or 3x the limit of detection

		TV		MG	
Media Type	**Panel Member**	**Percent Agreement**	**95% Exact CI of Percent Agreement**	**Percent Agreement**	**95% Exact CI of Percent Agreement**
PCR Media/Urine	~1.0x LoD TV, Negative MG	100.0 (216/216)	(98.3, 100.0)	Not Applicable	Not Applicable
	Negative TV, ~1.0x LoD MG	Not Applicable	Not Applicable	100.0 (216/216)	(98.3, 100.0)
	~3.0x LoD TV, ~1.0x LoD MG	100.0 (216/216)	(98.3, 100.0)	99.1 (214/216)	(96.7, 99.9)
	~1.0x LoD TV, ~3.0x LoD MG	99.1 (214/216)	(96.7, 99.9)	100.0 (216/216)	(98.3, 100.0)
PCR Media/ Vaginal Swab	~1.0x LoD TV, Negative MG	99.5 (215/216)	(97.4, 100.0)	Not Applicable	Not Applicable
	Negative TV, ~1.0x LoD MG	Not Applicable	Not Applicable	99.1 (214/216)	(96.7, 99.9)
	~3.0x LoD TV, ~1.0x LoD MG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	~1.0x LoD TV, ~3.0x LoD MG	98.6 (213/216)	(96.0, 99.7)	100.0 (216/216)	(98.3, 100.0)
PCR Media/ Meatal Swab	~1.0x LoD TV, Negative MG			Not Applicable	Not Applicable
	Negative TV, ~1.0x LoD MG			100.0 (216/216)	(98.3, 100.0)
	~3.0x LoD TV, ~1.0x LoD MG			99.5 (215/216)	(97.4, 100.0)
	~1.0x LoD TV, ~3.0x LoD MG			100.0 (216/216)	(98.3, 100.0)
PreservCyt®/ Cervical	~1.0x LoD TV, Negative MG	88.4 (190/215)	(83.3, 92.3)		
	Negative TV, ~1.0x LoD MG	Not Applicable	Not Applicable		
	~3.0x LoD TV, ~1.0x LoD MG	100.0 (215/215)	(98.3, 100.0)		
	~1.0x LoD TV, ~3.0x LoD MG	97.2 (210/216)	(94.1, 99.0)		

Note: CI = Confidence Interval; LoD= Limit of Detection; MG = *Mycoplasma genitalium*; TV = *Trichomonas vaginalis*.

5.2. Clinical study

The clinical performance of **cobas**® TV/MG was established in a multi-site, prospective study by comparing the results to a Patient Infected Status (PIS) that used a combination of FDA-cleared TV NAATs, TV culture, and 3 laboratory developed MG NAATs. Female and male urogenital specimens were collected from subjects enrolled at 10 geographically diverse sites in the US with testing performed at 6 laboratory testing sites (5 external and 1 internal).

Female subjects provided the following urogenital specimens: first-void urine, 1 self-collected and 4 clinician-collected vaginal swab specimens (self-collection arm of the study), or 5 clinician-collected vaginal swab specimens (clinician-collected arm of the study), a clinician-collected endocervical swab in **cobas**® PCR Media, and a cervical specimen in PreservCyt® Solution obtained with a spatula/cytobrush broom. If the female subject was in the self-collected arm of the study, then 1 vaginal swab was self-collected first and placed in **cobas**® PCR Media and then followed by 4 clinician-collected vaginal swabs transferred to the respective transport media collection devices. If the female subject was in the clinician-collected arm of the study, then 5 clinician-collected vaginal swabs were transferred to the respective transport media collection devices.

Male subjects provided the following urogenital specimens: 1 self-collected penile meatal swab (self-collection arm of the study) and urine, or 1 clinician-collected penile meatal swab (clinician-collected arm of the study) and urine. Each meatal swab was placed in **cobas**® PCR Media. Urine collected from each subject was placed in **cobas**® PCR Media and the respective transport media collection devices.

Subjects were classified as symptomatic if they self-reported symptoms or based on the discretion of the examining clinician were determined to have symptoms indicative of a TV or MG infection as listed below:

- Dysuria (pain and/or discomfort during urination)
- Coital pain, difficulty or bleeding
- Pelvic pain
- Any abnormal vaginal discharge
- Unusual vaginal odor
- Pelvic, uterine or ovarian pain

- Penile discharge
- Testicular pain
- Scrotal pain or swelling, itching, burning, redness, or soreness of genitals

Subjects were classified as asymptomatic based on the absence of symptoms.

Specimens were tested for TV and MG using **cobas**® TV/MG and the TV or MG assays determining the PIS. All tests were run according to the respective manufacturers Instructions for Use or as per the laboratory developed MG NAAT SOPs.

The clinical performance of **cobas**® TV/MG was evaluated by comparing the results from collected specimen types to a pre-specified PIS algorithm as determined by the combination of 2 commercially available tests (NAAT and culture) for TV and 3 laboratory developed NAATs for MG. The PIS algorithms were derived from the results of testing vaginal swabs in women and the results of testing urine in men for the determination of TV PIS and MG PIS respectively as shown in Table 21 and Table 22.

Table 21: Determination of TV PIS as derived from vaginal swabs and male urine

Culture	FDA-Cleared NAAT	Patient Infection Status (PIS)
+	+ / - / Invalid	Infected
+ / - / Invalid	+	Infected
-	-	Non-Infected
-	Invalid	Indeterminate
Invalid	-	Indeterminate
Invalid	Invalid	Indeterminate

Table 22: Determination of MG PIS as derived from vaginal swabs and male urine

		Lab developed NAAT2	Lab developed NAAT3		
			+	-	Invalid
Lab developed NAAT1	+	+	Infected	Infected	Infected
		-	Infected	Non-infected	Indeterminate
		Invalid	Infected	Indeterminate	Indeterminate
	-	+	Infected	Non-infected	Indeterminate
		-	Non-infected	Non-infected	Non-infected
		Invalid	Indeterminate	Non-infected	Indeterminate
	Invalid	+	Infected	Indeterminate	Indeterminate
		-	Indeterminate	Non-infected	Indeterminate
		Invalid	Indeterminate	Indeterminate	Indeterminate

Sensitivity (SENS), specificity (SPEC), positive predictive value (PPV), and negative predictive value (NPV) of **cobas**® TV/MG were calculated separately for the detection of TV or MG using the PIS as the composite reference standard and evaluated by gender, specimen type, and symptom status.

5.2.1. Results

A total of 2,194 subjects were enrolled and across all specimen types, 6807 samples were tested on of cobas® TV/MG, of which 12 samples had invalid results for TV and/or MG in the first run, hence an invalid rate of 0.18% (12/6807) with 95% Score CI of (0.10%, 0.31%)). Upon repeat testing of the 12 samples, 5 yielded valid results and 7 yielded invalid results.

From the total of 2,194 subjects enrolled, 2,154 were considered evaluable (1,108 females and 1,046 males) for TV and/or MG analyses. The 2,154 evaluable subjects contributed a total of 5,285 TV and 5,382 MG results across all specimen types.

5.2.1.1. TV clinical performance

Table 23 and Table 24 summarize the results by gender from symptomatic and asymptomatic subjects designated as Infected or Non-Infected with TV according to the PIS algorithm. A total of 171 females and 23 males were infected with valid TV result. Symptoms were reported in 67% (116/171) of infected and 56% (509/909) of non-infected females. Symptoms were reported in 56.5% (13/23) of infected and 31% (302/960) of non-infected males.

Table 23: TV positive/negative analyses for female PIS

	NAAT	Culture	cobas® TV/MG				Symptom Status		
Patient Infected Status	**VS**	**VS**	**UR**	**VS-C/ VS-S**	**PC**	**ES**	**Symp**	**Asymp**	**Total**
Infected	+	N/A	+	+	+	-	1	0	1
Infected	+	N/A	+	+	+	+	4	6	10
Infected	+	-	-	-	-	-	0	1	1
Infected	+	-	+	+	-	-	1	0	1
Infected	+	-	+	+	+	-	1	0	1
Infected	+	-	+	+	-	+	3	1	4
Infected	+	-	+	+	+	+	8	2	10
Infected	+	+	-	+	-	+	1	0	1
Infected	+	+	-	+	+	+	2	0	2
Infected	+	+	+	+	+	Failed	1	0	1
Infected	+	+	+	+	Failed	+	1	0	1
Infected	+	+	+	+	-	+	2	0	2
Infected	+	+	+	+	+	+	91	45	136
Total Infected							**116**	**55**	**171**
Non-Infected	-	-	N/A	-	-	-	1	0	1
Non-Infected	-	-	Invalid	-	-	-	2	0	2
Non-Infected	-	-	-	N/A	-	N/A	1	0	1
Non-Infected	-	-	-	Failed	-	N/A	1	0	1
Non-Infected	-	-	-	-	-	N/A	0	1	1
Non-Infected	-	-	-	-	+	N/A	1	0	1
Non-Infected	-	-	-	-	N/A	-	1	3	4
Non-Infected	-	-	-	Invalid	-	-	0	1	1
Non-Infected	-	-	-	-	-	-	476	368	844
Non-Infected	-	-	-	+	-	-	12	10	22
Non-Infected	-	-	-	-	+	-	1	2	3
Non-Infected	-	-	-	+	+	-	1	0	1
Non-Infected	-	-	-	-	-	+	5	6	11
Non-Infected	-	-	-	+	-	+	1	0	1
Non-Infected	-	-	-	-	+	+	0	1	1
Non-Infected	-	-	-	+	+	+	0	2	2
Non-Infected	-	-	+	-	-	-	5	3	8
Non-Infected	-	-	+	+	+	-	1	1	2
Non-Infected	-	-	+	-	-	+	0	1	1
Non-Infected	-	-	+	+	-	+	0	1	1
Total Non-Infected							**509**	**400**	**909**

Asymp = asymptomatic; Symp = symptomatic.
Note: Any positive result in vaginal swab specimen from females determines the PIS as 'Infected'. When both results are negative, the PIS is defined as 'Non-Infected'. Any subject with an invalid test result with either test must still have a positive test result for the remaining comparator test to be interpreted as PIS 'Infected'. If the remaining valid test is negative, in conjunction with an invalid test result, then the PIS is considered 'Indeterminate'.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with **cobas®** TV/MG for TV are considered evaluable and included in this summary table.
Note: + denotes Positive, - denotes Negative, N/A = data not available.
Note: VS = vaginal swab; VS-C = clinician-collected vaginal swab; VS-S = self-collected vaginal swab; UR = urine; PC = PreservCyt®; ES = endocervical swab.
Note: NAAT = nucleic acid amplification test; TV = *Trichomonas vaginalis*; MG = *Mycoplasma genitalium*.
Note: "Invalid" is a sample that either had an instrument amplification/detection error or whose result was excluded due to a protocol deviation.
Note: "Failed" is a sample that had an instrument processing error.

Table 24: TV positive/negative analyses for male PIS

	NAAT	Culture	cobas® TV/MG	Symptom Status		
Patient Infected Status	**UR**	**UR**	**UR**	**Symp**	**Asymp**	**Total**
Infected	+	N/A	+	0	1	1
Infected	+	-	+	3	3	6
Infected	+	+	+	10	6	16
Total Infected				**13**	**10**	**23**
Non-Infected	-	-	-	297	648	945
Non-Infected	-	-	+	5	10	15
Total Non-Infected				**302**	**658**	**960**

Symp = symptomatic, Asymp = asymptomatic.
Note: Any positive result in urine specimen from males determines the PIS as 'Infected'. When both results are negative, the PIS is defined as Non-Infected'. Any subject with an invalid test result with either test must still have a positive test result for the remaining comparator test to be interpreted as PIS 'Infected'. If the remaining valid test is negative in conjunction with an invalid test result, then the PIS is considered 'Indeterminate'.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with **cobas®** TV/MG for TV are considered evaluable and included in this summary table.
Note: + denotes Positive, - denotes Negative, N/A = data not available.
Note: UR = urine.
Note: MG = *Mycoplasma genitalium*, NAAT = nucleic acid amplification test, TV = *Trichomonas vaginalis*.

Sensitivity, specificity, and predictive values of **cobas**® TV/MG for TV as defined by PIS are presented by gender, specimen type, and symptom status in Table 25.

Table 25: TV clinical performance compared with PIS by gender, specimen type, and symptom status

Sample Type[a]	Symptom Status[b]	Total (n)	SENS	95% Score CI	SPEC	95% Score CI	PREV (%)	PPV (%)	NPV (%)
Female									
UR	Symp	622	97.4% (113/116)	(92.7%, 99.1%)	98.8% (500/506)	(97.4%, 99.5%)	18.6	95.0	99.4
	Asymp	455	98.2% (54/55)	(90.4%, 99.7%)	98.5% (394/400)	(96.8%, 99.3%)	12.1	90.0	99.7
	Overall	1077	97.7% (167/171)	(94.1%, 99.1%)	98.7% (894/906)	(97.7%, 99.2%)	15.9	93.3	99.6
VS-C/ VS-S	Symp	623	100.0% (116/116)	(96.8%, 100.0%)	97.0% (492/507)	(95.2%, 98.2%)	18.6	88.5	100.0
	Asymp	454	98.2% (54/55)	(90.4%, 99.7%)	96.5% (385/399)	(94.2%, 97.9%)	12.1	79.4	99.7
	Overall	1077	99.4% (170/171)	(96.8%, 99.9%)	96.8% (877/906)	(95.4%, 97.8%)	15.9	85.4	99.9
PC	Symp	622	93.9% (108/115)	(88.0%, 97.0%)	99.2% (503/507)	(98.0%, 99.7%)	18.5	96.4	98.6
	Asymp	452	96.4% (53/55)	(87.7%, 99.0%)	98.5% (391/397)	(96.7%, 99.3%)	12.2	89.8	99.5
	Overall	1074	94.7% (161/170)	(90.2%, 97.2%)	98.9% (894/904)	(98.0%, 99.4%)	15.8	94.2	99.0
ES	Symp	620	97.4% (112/115)	(92.6%, 99.1%)	98.8% (499/505)	(97.4%, 99.5%)	18.5	94.9	99.4
	Asymp	454	98.2% (54/55)	(90.4%, 99.7%)	97.2% (388/399)	(95.1%, 98.5%)	12.1	83.1	99.7
	Overall	1074	97.6% (166/170)	(94.1%, 99.1%)	98.1% (887/904)	(97.0%, 98.8%)	15.8	90.7	99.6
Male									
UR	Symp	315	100.0% (13/13)	(77.2%, 100.0%)	98.3% (297/302)	(96.2%, 99.3%)	4.1	72.2	100.0
	Asymp	668	100.0% (10/10)	(72.2%, 100.0%)	98.5% (648/658)	(97.2%, 99.2%)	1.5	50.0	100.0
	Overall	983	100.0% (23/23)	(85.7%, 100.0%)	98.4% (945/960)	(97.4%, 99.1%)	2.3	60.5	100.0

[a] ES = endocervical swab; PC = PreservCyt®; UR = urine; VS-C = clinician-collected vaginal swab; VS-S = self-collected vaginal swab.
[b] Asymp = asymptomatic; Symp = symptomatic.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with **cobas®** TV/MG for TV are considered evaluable and included in this summary table.
Note: CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value; PREV = prevalence; SENS = sensitivity; SPEC = specificity.

5.2.1.2. Expected values for TV

5.2.1.2.1. Positivity Rate

Table 26: TV positivity rate of cobas TV/MG observed during the study

Sample Type[a]	Symptom Status[b]	Total (n)	cobas TV Positive Result	Positivity Rate	95% Score CI
Female					
UR	Symp	622	119	19.1%	(16.2%, 22.4%)
	Asymp	455	60	13.2%	(10.4%, 16.6%)
	Overall	1077	179	16.6%	(14.5%, 19.0%)
VS-C/ VS-S	Symp	623	131	21.0%	(18.0%, 24.4%)
	Asymp	454	68	15.0%	(12.0%, 18.6%)
	Overall	1077	199	18.5%	(16.3%, 20.9%)
PC	Symp	622	112	18.0%	(15.2%, 21.2%)
	Asymp	452	59	13.1%	(10.3%, 16.5%)
	Overall	1074	171	15.9%	(13.9%, 18.2%)
ES	Symp	620	118	19.0%	(16.1%, 22.3%)
	Asymp	454	65	14.3%	(11.4%, 17.8%)
	Overall	1074	183	17.0%	(14.9%, 19.4%)
Male					
UR	Symp	315	18	5.7%	(3.6%, 8.9%)
	Asymp	668	20	3.0%	(1.9%, 4.6%)
	Overall	983	38	3.9%	(2.8%, 5.3%)

[a] UR = urine, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal swab, PC = PreservCyt, ES = endocervical swab.
[b] Symp = symptomatic, Asymp = asymptomatic.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with cobas TV/MG for TV are considered evaluable and included in this summary table.
Note: CI = confidence interval.

5.2.1.2.2. Positive and negative predictive values for TV

Hypothetical positive and negative predictive values (PPV and NPV) of **cobas**® TV/MG derived from disease prevalence of 1 to 50% are shown in Table 27 through Table 31, respectively, per specimen type.

Table 27: Positive Predictive Value and Negative Predictive Value for hypothetical TV prevalence - female urine

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	97.7	98.7	42.69	99.98
3	97.7	98.7	69.52	99.93
5	97.7	98.7	79.51	99.88
10	97.7	98.7	89.12	99.74
15	97.7	98.7	92.86	99.58

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
20	97.7	98.7	94.85	99.41
30	97.7	98.7	96.93	98.99
50	97.7	98.7	98.66	97.68

Note: NPV = Negative predictive value ; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

Table 28: Positive Predictive Value and Negative Predictive Value for hypothetical TV prevalence - vaginal swab

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	99.4	96.8	23.88	99.99
3	99.4	96.8	48.99	99.98
5	99.4	96.8	62.04	99.97
10	99.4	96.8	77.53	99.93
15	99.4	96.8	84.57	99.89
20	99.4	96.8	88.59	99.85
30	99.4	96.8	93.01	99.74
50	99.4	96.8	96.88	99.40

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

Table 29: Positive Predictive Value and Negative Predictive Value for hypothetical TV prevalence - PreservCyt®

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	94.7	98.9	46.37	99.95
3	94.7	98.9	72.59	99.83
5	94.7	98.9	81.84	99.72
10	94.7	98.9	90.49	99.41
15	94.7	98.9	93.79	99.06
20	94.7	98.9	95.54	98.68
30	94.7	98.9	97.35	97.76
50	94.7	98.9	98.85	94.92

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

Table 30: Positive Predictive Value and Negative Predictive Value for hypothetical TV prevalence - endocervical swab

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	97.6	98.1	34.40	99.98
3	97.6	98.1	61.63	99.93
5	97.6	98.1	73.21	99.87
10	97.6	98.1	85.23	99.73
15	97.6	98.1	90.16	99.58
20	97.6	98.1	92.85	99.40
30	97.6	98.1	95.70	98.98
50	97.6	98.1	98.11	97.66

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

Table 31: Positive Predictive Value and Negative Predictive Value for hypothetical TV prevalence - male urine

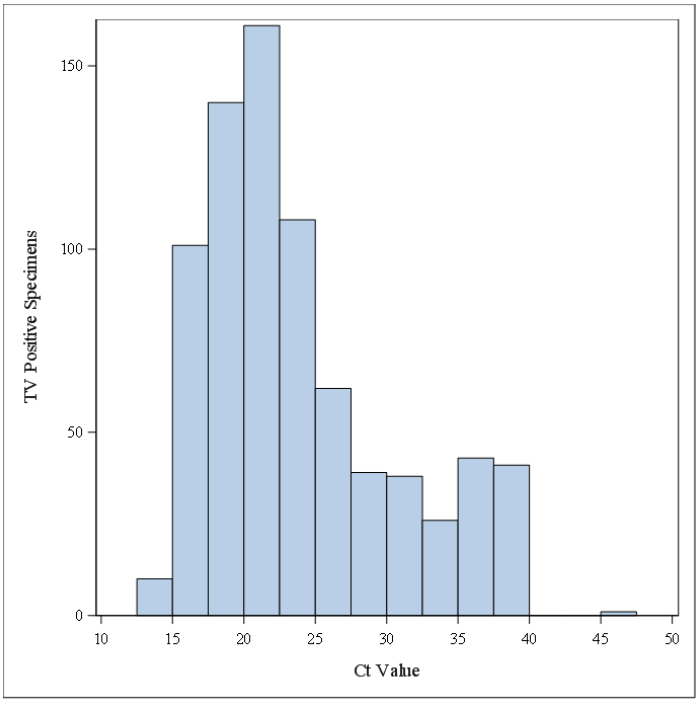
Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	100.0	98.4	39.26	100.0
3	100.0	98.4	66.44	100.0
5	100.0	98.4	77.11	100.0
10	100.0	98.4	87.67	100.0
15	100.0	98.4	91.87	100.0
20	100.0	98.4	94.12	100.0
30	100.0	98.4	96.48	100.0
50	100.0	98.4	98.46	100.0

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

5.2.1.3. Cycle threshold frequency distribution for TV

A total of 770 specimens (combined female and male) were positive for TV. The frequency distribution of Ct values from **cobas**® TV/MG positive results for TV infected specimens are shown in Figure 2.

Figure 2: Cycle threshold distribution of TV positive specimens



5.2.1.4. MG clinical performance

Table 32 and Table 33 summarize the results from gender by symptomatic and asymptomatic subjects designated as infected or non-infected with MG according to the PIS algorithm. A total of 59 females and 60 males were infected with MG. Symptoms were reported in 67% (40/59) of infected and 57% (601/1045) of non-infected females. Symptoms were reported in 52% (31/60) of infected and 32% (312/986) of non-infected males.

Table 32: MG positive/negative analysis for female PIS

	NAAT1	NAAT2	NAAT3	cobas TV/MG			Symptom Status		
Patient Infected Status	**VS**	**VS**	**VS**	**UR**	**VS-C/ VS-S**	**ES**	**Symp**	**Asymp**	**Total**
Infected	-	+	+	-	-	-	0	1	1
Infected	-	+	+	-	+	+	4	1	5
Infected	-	+	+	+	+	-	4	1	5
Infected	-	+	+	+	+	+	7	4	11
Infected	+	-	+	-	-	-	1	0	1
Infected	+	-	+	+	+	+	1	1	2
Infected	+	+	+	-	+	+	1	0	1
Infected	+	+	+	+	+	-	1	2	3
Infected	+	+	+	+	+	+	21	9	30
Total Infected							40	19	59
Non-Infected	-	-	Invalid	-	-	+	1	0	1
Non-Infected	-	-	-	N/A	-	-	1	0	1
Non-Infected	-	-	-	Invalid	Invalid	-	1	0	1
Non-Infected	-	-	-	Invalid	-	-	3	0	3
Non-Infected	-	-	-	-	Failed	N/A	1	0	1
Non-Infected	-	-	-	-	-	N/A	1	0	1
Non-Infected	-	-	-	-	-	Failed	1	0	1
Non-Infected	-	-	-	-	Invalid	-	0	1	1
Non-Infected	-	-	-	-	-	-	533	422	955
Non-Infected	-	-	-	-	-	+	1	0	1
Non-Infected	-	-	-	+	-	-	3	0	3
Non-Infected	-	-	+	-	-	-	12	2	14
Non-Infected	-	-	+	-	+	-	6	2	8
Non-Infected	-	-	+	-	-	+	2	1	3
Non-Infected	-	-	+	-	+	+	1	1	2
Non-Infected	-	-	+	+	-	-	6	1	7
Non-Infected	-	-	+	+	+	-	6	5	11
Non-Infected	-	-	+	+	+	+	9	1	10
Non-Infected	-	+	-	-	-	N/A	0	1	1
Non-Infected	-	+	-	-	-	-	7	1	8
Non-Infected	+	-	-	-	-	-	6	6	12
Total Non-Infected							601	444	1045

	NAAT1	NAAT2	NAAT3	cobas TV/MG			Symptom Status		
Patient Infected Status	**VS**	**VS**	**VS**	**UR**	**VS-C/ VS-S**	**ES**	**Symp**	**Asymp**	**Total**

Note: Symp = symptomatic, Asymp = asymptomatic.
Note: Two or more positive results in vaginal swab specimens from females determines the PIS as 'Infected'. Any other combination of valid results defines their PIS as 'Non-Infected'. If one of the NAATs is invalid, the two remaining NAAT results must be concordant positive (+) or concordant negative (-) for the PIS to be 'Infected' or 'Non-Infected', respectively. For any other combination of invalid results PIS is considered 'Indeterminate'.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with cobas TV/MG for MG are considered evaluable and included in this summary table.
Note: + denotes Positive, - denotes Negative, N/A = data not available.
Note: UR = urine, VS = vaginal swab, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal swab, ES = endocervical swab.
Note: NAAT = nucleic acid amplification test, TV = Trichomonas vaginalis, MG = Mycoplasma genitalium.
Note: "Invalid" is a sample that either had an instrument amplification/detection error or whose result was excluded due to a protocol deviation.
Note: "Failed" is a sample that had an instrument processing error.

Table 33: MG positive/negative analysis for male PIS

	NAAT1	NAAT2	NAAT3	cobas® TV/MG		Symptom Status		
Patient Infected Status	UR	UR	UR	UR	MS-C/ MS-S	Symp	Asymp	Total
Infected	-	+	+	+	-	1	1	2
Infected	-	+	+	+	+	1	1	2
Infected	+	-	+	+	-	0	1	1
Infected	+	-	+	+	+	3	5	8
Infected	+	+	-	+	+	0	1	1
Infected	+	+	+	+	-	2	4	6
Infected	+	+	+	+	+	24	16	40
Total Infected						**31**	**29**	**60**
Non-Infected	N/A	-	-	-	-	2	1	3
Non-Infected	-	Invalid	-	-	-	0	2	2
Non-Infected	-	-	N/A	-	-	0	1	1
Non-Infected	-	-	-	N/A	-	0	1	1
Non-Infected	-	-	-	-	N/A	0	4	4
Non-Infected	-	-	-	-	Failed	0	1	1
Non-Infected	-	-	-	-	Invalid	0	2	2
Non-Infected	-	-	-	-	-	288	634	922
Non-Infected	-	-	-	-	+	3	3	6
Non-Infected	-	-	-	+	+	1	1	2
Non-Infected	-	-	+	-	-	0	2	2
Non-Infected	-	-	+	-	+	1	0	1
Non-Infected	-	-	+	+	Invalid	0	1	1
Non-Infected	-	-	+	+	-	2	6	8
Non-Infected	-	-	+	+	+	5	6	11
Non-Infected	-	+	-	-	-	1	4	5
Non-Infected	-	+	-	+	-	1	0	1
Non-Infected	+	-	-	-	-	7	5	12
Non-Infected	+	-	-	+	+	1	0	1
Total Non-Infected						**312**	**674**	**986**

Asymp = asymptomatic; Symp = symptomatic.
Note: Two or more positive results in urine specimens from males determines the PIS as 'Infected'. Any other combination of valid results defines their PIS as 'Non-Infected'. If one of the NAATs is invalid, the two remaining NAAT results must be concordant positive (+) or concordant negative (-) for the PIS to be 'Infected' or 'Non-Infected', respectively. For any other combination of invalid results PIS is considered 'Indeterminate'.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with **cobas®** TV/MG for MG are considered evaluable and included in this summary table.
Note: + denotes Positive, - denotes Negative, N/A = data not available.
Note: MS-C = clinician-collected meatal swab; MS-S = self-collected meatal swab; UR = urine.
Note: MG = *Mycoplasma genitalium;* NAAT = nucleic acid amplification test; TV = *Trichomonas vaginalis*.
Note: "Invalid" is a sample that either had an instrument amplification/detection error or whose result was excluded due to a protocol deviation.
Note: "Failed" is a sample that had an instrument processing error.

Sensitivity, specificity, and predictive values of **cobas**® TV/MG for MG as defined by PIS are presented by gender, specimen type, and symptom status in Table 34.

Table 34: MG clinical performance compared with PIS by gender, specimen type, and symptom status

Sample Type[a]	Symptom Status[b]	Total (n)	SENS	95% Score CI	SPEC	95% Score CI	PREV (%)	PPV (%)	NPV (%)
Female									
UR	Symp	636	85.0% (34/40)	(70.9%, 92.9%)	96.0% (572/596)	(94.1%, 97.3%)	6.3	58.6	99.0
	Asymp	463	89.5% (17/19)	(68.6%, 97.1%)	98.4% (437/444)	(96.8%, 99.2%)	4.1	70.8	99.5
	Overall	1099	86.4% (51/59)[c]	(75.5%, 93.0%)	97.0% (1009/1040)	(95.8%, 97.9%)	5.4	62.2	99.2
VS-C/ VS-S	Symp	639	97.5% (39/40)	(87.1%, 99.6%)	96.3% (577/599)	(94.5%, 97.6%)	6.3	63.9	99.8
	Asymp	462	94.7% (18/19)	(75.4%, 99.1%)	98.0% (434/443)	(96.2%, 98.9%)	4.1	66.7	99.8
	Overall	1101	96.6% (57/59)[d]	(88.5%, 99.1%)	97.0% (1011/1042)	(95.8%, 97.9%)	5.4	64.8	99.8
ES	Symp	637	85.0% (34/40)	(70.9%, 92.9%)	97.7% (583/597)	(96.1%, 98.6%)	6.3	70.8	99.0
	Asymp	462	78.9% (15/19)	(56.7%, 91.5%)	99.3% (440/443)	(98.0%, 99.8%)	4.1	83.3	99.1
	Overall	1099	83.1% (49/59)[e]	(71.5%, 90.5%)	98.4% (1023/1040)	(97.4%, 99.0%)	5.4	74.2	99.0
Male									
UR	Symp	343	100.0% (31/31)	(89.0%, 100.0%)	96.8% (302/312)	(94.2%, 98.2%)	9.0	75.6	100.0
	Asymp	702	100.0% (29/29)	(88.3%, 100.0%)	97.9% (659/673)	(96.5%, 98.8%)	4.1	67.4	100.0
	Overall	1045	100.0% (60/60)	(94.0%, 100.0%)	97.6% (961/985)	(96.4%, 98.4%)	5.7	71.4	100.0
MS-C/ MS-S	Symp	343	90.3% (28/31)	(75.1%, 96.7%)	96.5% (301/312)	(93.8%, 98.0%)	9.0	71.8	99.0
	Asymp	695	79.3% (23/29)	(61.6%, 90.2%)	98.5% (656/666)	(97.3%, 99.2%)	4.2	69.7	99.1
	Overall	1038	85.0% (51/60)[f]	(73.9%, 91.9%)	97.9% (957/978)	(96.7%, 98.6%)	5.8	70.8	99.1

Sample Type[a]	Symptom Status[b]	Total (n)	SENS	95% Score CI	SPEC	95% Score CI	PREV (%)	PPV (%)	NPV (%)

[a] ES = endocervical swab; MS-C = clinician-collected meatal swab; MS-S = self-collected meatal swab; UR = urine; VS-C = clinician-collected vaginal swab; VS-S = self-collected vaginal swab.
[b] Asymp = asymptomatic; Symp = symptomatic.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with **cobas®** TV/MG for MG are considered evaluable and included in this summary table.
Note: CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value; PREV = prevalence; SENS = sensitivity; SPEC = specificity.

5.2.1.5. Expected values for MG

5.2.1.5.1. Positivity Rate

Table 35: MG positivity rate of cobas TV/MG observed during the study

Sample Type[a]	Symptom Status[b]	Total (n)	cobas® MG Positive Result	Positivity Rate	95% Score CI
Female					
UR	Symp	636	58	9.1%	(7.1%, 11.6%)
	Asymp	463	24	5.2%	(3.5%, 7.6%)
	Overall	1099	82	7.5%	(6.1%, 9.2%)
VS-C/ VS-S	Symp	639	61	9.5%	(7.5%, 12.1%)
	Asymp	462	27	5.8%	(4.0%, 8.4%)
	Overall	1101	88	8.0%	(6.5%, 9.7%)
ES	Symp	637	48	7.5%	(5.7%, 9.8%)
	Asymp	462	18	3.9%	(2.5%, 6.1%)
	Overall	1099	66	6.0%	(4.7%, 7.6%)

Sample Type[a]	Symptom Status[b]	Total (n)	cobas® MG Positive Result	Positivity Rate	95% Score CI
Male					
UR	Symp	343	41	12.0%	(8.9%, 15.8%)
	Asymp	702	43	6.1%	(4.6%, 8.1%)
	Overall	1045	84	8.0%	(6.5%, 9.8%)
MS-C/ MS-S	Symp	343	39	11.4%	(8.4%, 15.2%)
	Asymp	695	33	4.7%	(3.4%, 6.6%)
	Overall	1038	72	6.9%	(5.5%, 8.6%)

Sample Type[a]	Symptom Status[b]	Total (n)	cobas® MG Positive Result	Positivity Rate	95% Score CI

[a] ES = endocervical swab, MS-C = clinician-collected meatal swab, MS-S = self-collected meatal swab; UR = urine, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal swab,
[b] Asymp = asymptomatic; Symp = symptomatic.
Note: Subjects with a designated patient infection status (Infected or Non-Infected) and a valid test result with **cobas®** TV/MG for MG are considered evaluable and included in this summary table.
Note: CI = confidence interval.

5.2.1.5.2. Positive and negative predictive values for MG

Hypothetical positive and negative predictive values (PPV and NPV) of cobas® TV/MG derived from disease prevalence of 1 to 50% are shown in Table 36 through Table 40, respectively, per specimen type.

Table 35: Positive Predictive Value and Negative Predictive Value for hypothetical MG prevalence - female urine

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	86.4	97.0	22.66	99.86
3	86.4	97.0	47.28	99.57
5	86.4	97.0	60.42	99.27
10	86.4	97.0	76.32	98.47
15	86.4	97.0	83.65	97.59
20	86.4	97.0	87.88	96.62
30	86.4	97.0	92.55	94.35
50	86.4	97.0	96.67	87.74

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas®** TV/MG to patient infected status.

Table 36: Positive Predictive Value and Negative Predictive Value for hypothetical MG prevalence - vaginal swab

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	96.6	97.0	24.70	99.96
3	96.6	97.0	50.11	99.89
5	96.6	97.0	63.09	99.82
10	96.6	97.0	78.30	99.61
15	96.6	97.0	85.14	99.39
20	96.6	97.0	89.03	99.13
30	96.6	97.0	93.30	98.52
50	96.6	97.0	97.01	96.62

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

Table 37: Positive Predictive Value and Negative Predictive Value for hypothetical MG prevalence - endocervical swab

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	83.1	98.4	33.92	99.83
3	83.1	98.4	61.11	99.47
5	83.1	98.4	72.78	99.10
10	83.1	98.4	84.95	98.12
15	83.1	98.4	89.97	97.05
20	83.1	98.4	92.70	95.87
30	83.1	98.4	95.61	93.12
50	83.1	98.4	98.07	85.30

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

Table 38: Positive Predictive Value and Negative Predictive Value for hypothetical MG prevalence - male urine

Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	100.0	97.6	29.31	100.0
3	100.0	97.6	55.93	100.0
5	100.0	97.6	68.36	100.0
10	100.0	97.6	82.02	100.0
15	100.0	97.6	87.87	100.0
20	100.0	97.6	91.12	100.0
30	100.0	97.6	94.62	100.0
50	100.0	97.6	97.62	100.0

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

Table 39: Positive Predictive Value and Negative Predictive Value for hypothetical MG prevalence - meatal swab

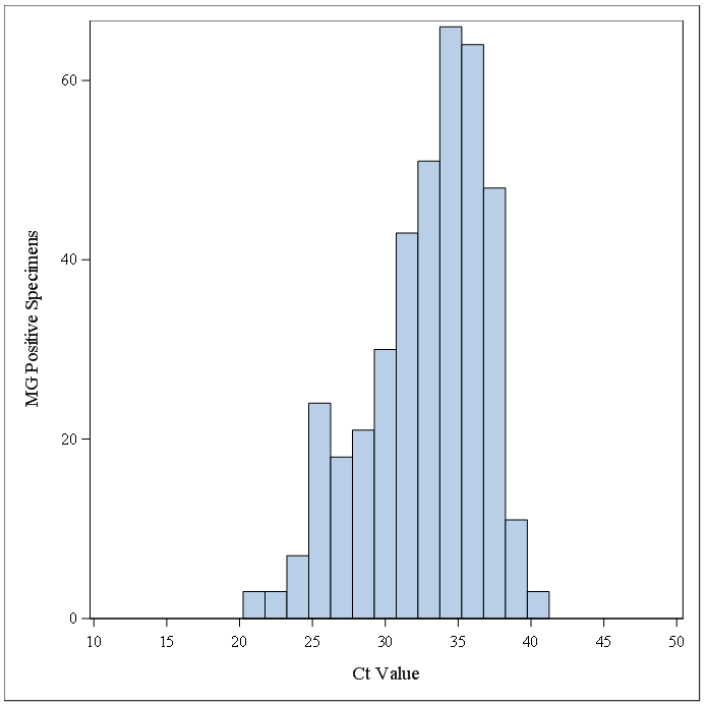
Prevalence (%)	Sensitivity[a] (%)	Specificity[a] (%)	PPV (%)	NPV (%)
1	85.0	97.9	28.56	99.85
3	85.0	97.9	55.04	99.53
5	85.0	97.9	67.57	99.20
10	85.0	97.9	81.48	98.33
15	85.0	97.9	87.48	97.37
20	85.0	97.9	90.82	96.31
30	85.0	97.9	94.43	93.84
50	85.0	97.9	97.54	86.71

Note: NPV = Negative predictive value; PPV = Positive predictive value.
[a]The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

5.2.1.6. Cycle threshold frequency distribution for MG

A total of 392 specimens (combined female and male) were positive for MG. The frequency distribution of Ct values from **cobas**® TV/MG positive results for MG infected specimens are shown in Figure 3.

Figure 3: Cycle threshold distribution of MG positive specimens



5.3. Specimen-specific agreement for the detection of MG

A study was conducted with prospectively collected female and male urogenital specimens from 836 subjects (412 females and 424 males). This study analyzed the performance of **cobas**® TV/MG for the detection of MG in female (urine, vaginal swab, and endocervical swab) and male (urine and meatal swab) specimen types with respect to an anatomic site-specific composite reference standard (i.e., **cobas**® TV/MG urine results were compared to a urine-specific composite reference, and the same for the other female and male specimen types). The composite reference standard was comprised of 3 MG NAATs where the determination of truth was based on any 2 positive tests out of the 3 MG reference NAATs used.

Table 41 MG Positive and Negative Percent Agreement of cobas® TV/MG with anatomic site-specific composite reference

Sample Type[a]	ASCR[b]+/ cobas +	ASCR[b]-/ cobas +	ASCR[b]-/ cobas -	ASCR[b]+/ cobas -	PPA (95% Exact CI)	NPA (95% Exact CI)
Female						
UR	29	6	377	0	100% (88.1%, 100%)	98.4% (96.6%, 99.4%)
VS-C/ VS-S	27	2	381	2	93.1% (77.2%, 99.2%)	99.5% (98.1%, 99.9%)
ES	18	2	391	1	94.7% (74.0%, 99.9%)	99.5% (98.2%, 99.9%)
Male						
UR	39	5	380	0	100% (91.0%, 100%)	98.7% (97.0%, 99.6%)
MS-C/ MS-S	25	3	396	0	100% (86.3%, 100%)	99.2% 97.8%, 99.8%)

[a] ES = endocervical swab, MS-C = clinician-collected meatal swab, MS-S = self-collected meatal swab; UR = urine, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal swab.
[b] ASCR = Anatomic Site-specific Composite Reference (i.e., cobas TV/MG urine results were compared to a urine-specific composite reference, and the same for the other female and male specimen types).
Note: CI = confidence interval, PPA = positive percent agreement; NPA = negative percent agreement.

6. CONCLUSIONS

A comparison of the intended use, technological characteristics, and the results of non-clinical analytical and clinical performance studies demonstrate that **cobas®** TV/MG for use on the **cobas®** 6800/8800 systems is substantially equivalent to the predicate device.