Rx Only

cobas® TV/MG

Qualitative nucleic acid test
for use on the cobas® 5800/6800/8800 Systems

For in vitro diagnostic use

cobas® TV/MG	P/N: 09040633190
For use on the cobas® 5800 System	
cobas® TV/MG Positive Control Kit	P/N: 09040641190
cobas® Buffer Negative Control Kit	P/N: 09051953190
For use on the cobas® 6800/8800 Systems	
cobas® TV/MG Positive Control Kit	P/N: 07948689190 or P/N: 09040641190
cobas® Buffer Negative Control Kit	P/N: 07002238190 or P/N: 09051953190

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Intended use

cobas® TV/MG on the **cobas**® 5800/6800/8800 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 and female urine, clinician instructed self-collected vaginal swab specimens, 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 clinician instructed self-collected meatal swab specimens 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.

Summary and explanation of the test

Background

Trichomonas vaginalis is the most common non-viral sexually transmitted infection (STI) in the world, with an estimated 276.4 million cases in 2008 with an approximate prevalence in females and males of 8.1% and 1.0%, respectively.[1] However, these rates are thought to be an underestimation because most of the studies have been from methods such as wet mount microscopy versus nucleic acid amplification tests (NAATs). Global population based studies show rates ranging from 3.2% to 42.6%, depending on the geographic region studied.[1] *Trichomonas vaginalis* is also the most prevalent STI in the United States (US). A population-based study demonstrated an overall prevalence of 3.1% among women aged 14 to 49 years, with rates as high as 13.3% among black women in the general population.[2] Another study found TV prevalence of 11.9% in women aged 36 to 45, 7.7% in women aged 51 to 60, and 4.2% in women aged 16 to 25 years.[3] Molecular based tests for the detection of TV have shown a detection rate between 7% and 13% among females.[4] However, TV is currently not a reportable disease, and the true estimation of disease prevalence is not currently known. Some of the factors contributing to this are the lack of routine testing, low sensitivity (SENS) of the traditional laboratory tests, and non-specific symptomatology.

Trichomonas vaginalis is a parasitic protozoan that is approximately 10 to 20 µm in length and 2 to 14 µm in width, and it has four anterior flagella. *Trichomonas vaginalis* trophozoites divide by binary fission, and, in natural infections, give rise to a population in the lumen and on the mucosal surfaces of the urogenital tract of humans.[5] *Trichomonas vaginalis* primarily infects the squamous epithelial cells and erythrocytes and resides in the lower genital tract in females and in the male urethra and prostate in males.[1] Humans are the only known host for TV, and the pathogen is primarily sexually transmitted. Infection may persist for long periods (months to years) in women, but, in males, it generally persists less than ten days.

Women who are symptomatic for a TV infection complain of vaginal discharge, pruritus, and irritation. Other signs of infection include malodor, edema, and/or erythema. *Trichomonas vaginalis* is also known to cause urethritis in men who have sex with women. Men with trichomoniasis may feel itching or irritation inside the penis or burning after urination or ejaculation or have some discharge from the penis. Sviden et al observed a TV polymerase chain reaction (PCR) detection

rate of 8.2% in 500 men with urethritis versus a 2.2% detection rate in asymptomatic males.[4]

Laboratory diagnosis has relied on viewing the organisms under the microscope via a saline wet mount prepared from the patient's discharge. The motile trichomonads can be observed; however, the wet mount microscopy must be analyzed within 10 to 20 minutes of sample collection as the organism will lose viability, and, therefore, the characteristic motility. Another caveat of wet mount microscopy is that white blood cells (WBCs) are often in the vaginal fluid collected, and WBCs can be mistaken for TV organisms. So, although wet mount microscopy is quick and inexpensive, there is limited SENS, which ranges from 60% to 70%.[5,6]

The current gold standard for the laboratory diagnosis of TV is culture that can be performed in Diamond's medium. The commercially available, United States Food and Drug Administration (FDA)-approved InPouch™ TV (Biomed Diagnostics) is available for culture-based testing. Although the culture medium helps to maintain the viability of the TV organism, this testing remains relatively insensitive (73.3%).[6] Nucleic acid amplification testing has been shown to be more sensitive than the culture testing.[7]

The Centers for Disease Control and Prevention (CDC) recommends that women who test positive for TV be rescreened 3 months after treatment.[8] The CDC also recommends that women with human immunodeficiency virus (HIV) infection also be screened for TV at the initial visit and annually thereafter.

Mycoplasma genitalium is a fastidious bacterium first isolated in 1980 from the urethral swabs of two symptomatic men with non-gonococcal urethritis (NGU).[9] Infections caused by this bacterium have been associated with male and female urethritis, balanoposthitis, prostatitis, cervicitis, pelvic inflammatory disease, and male and female infertility.[10] Additional complications, such as preterm delivery and extra-genital infections, have been reported.

There have been few studies showing an accurate prevalence of MG because, historically, this bacterium is difficult to culture. However, a number of molecular assays have been described that show a prevalence as high as 47.5%.[11] Some of the factors accounting for the wide range in prevalence are related to the sample type (vaginal swab, urine, rectal swabs, or endocervical swabs) collected and the subjects selected. A recent study performed in 2016 from various public health clinics, family planning clinics, and hospital systems across the US using molecular methods showed the rates of prevalence at 16.3% and 17.2% for females and males, respectively.[12] Another study performed at a STI clinic showed that 17.5% of women tested positive for MG and that vaginal swabs have the highest relative SENS (85.7%), with urine samples showing a 61.4% relative SENS.[13] Mezzini et al showed that 8.1% (96/1,182) males who presented to a public sexual health clinic with symptoms of dysuria and/or urethral discharge had MG deoxyribonucleic acid (DNA) detected in their urine.[14]

Currently, there is no evidence-based consensus or gold-standard test for MG or a consensus sample type(s) to be collected. There are also no recommended guidelines for MG screening or testing, and the lack of a universally accepted, standardized assay complicates screening efforts for at-risk patient populations. Similar to TV, MG is not a reportable disease, and it is likely that, without laboratory testing available, some cases of MG infection are treated empirically as a *Chlamydia trachomatis* (CT) infection. There are also no recommended guidelines for retesting patients who have completed treatment for MG, although follow-up testing and reassessment may be indicated, depending on the patient's risk factors for re-infection and the history of and compliance with antibiotic treatment. Contributing to the potential need for retesting is the increased incidence of macrolide resistance when first line treatment may not work or work sub-optimally.[12]

Explanation of the test

cobas® TV/MG for use on the **cobas**® 5800 System, **cobas**® 6800 System or **cobas**® 8800 System (referred to as **cobas**® TV/MG throughout the remainder of this document) is an automated, qualitative real-time PCR test designed to detect

TV and MG DNA in urogenital specimens from male and female patients and thus fulfills the medical need for a rapid, high throughput molecular screening test for use as an aid in the diagnosis of TV and MG caused disease in both symptomatic and asymptomatic individuals. **cobas**® TV/MG enables the detection of TV and/or MG DNA in endocervical, vaginal, urine and cervical specimens of female patients and meatal and urine specimens of male patients. 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 a low titer positive and a negative control.

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**® 5800 System is designed as one integrated instrument. 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**® 5800 System or **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, external controls and added internal control DNA (DNA-IC) molecules is simultaneously extracted. In summary, bacterial 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.

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 uses two sets targeting separated 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 deoxythimidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon). Any contaminating amplicon from previous PCR runs are eliminated by the AmpErase enzyme, which is included in the PCR master mix, during the first thermal cycling step.[15] However, newly formed amplicon 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.[16,17] 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.

Reagents and materials

cobas® TV/MG reagents and controls

All unopened reagents and controls shall be stored as recommended in Table 1 to Table 4.

Table 1 cobas® TV/MG

(cobas® TV/MG)

Store at 2-8°C

384 test cassette (P/N 09040633190)

Kit components	Reagent ingredients	Quantity per kit 384 tests
Proteinase Solution (PASE)	Tris buffer, < 0.05% EDTA, Calcium chloride, Calcium acetate, 8% Proteinase EUH210: Safety data sheet available on request. EUH208: Contains subtilisin from Bacillus subtilis. May produce an allergic reaction.	38 mL
DNA Internal Control (DNA-IC)	Tris buffer, < 0.05% EDTA, < 0.001% non-TV/MG related DNA construct containing primer and probe specific sequence regions, < 0.1% Sodium azide	38 mL
Elution Buffer (EB)	Tris buffer, 0.2% Methyl-4 hydroxibenzoate	38 mL
Master Mix Reagent 1 (MMX-R1)	Manganese acetate, Potassium hydroxide, < 0.1% Sodium azide	14.5 mL
TV/MG Master Mix Reagent 2 (TV/MG MMX-R2)	Tricine buffer, Potassium acetate, EDTA, Glycerol, < 18% Dimethyl sulfoxide, < 0.12% dATP, dCTP, dGTP, dUTPs, < 0.1% Tween 20, < 0.1% Sodium azide, < 0.1% Z05 DNA polymerase, < 0.1% AmpErase (uracil-N glycosylase) enzyme (microbial), < 0.01% Internal Control forward and reverse primers, < 0.01% Upstream and downstream TV/MG primers, < 0.01% Fluorescent-labeled oligonucleotide probes specific for TV, MG and the DNA Internal Control, < 0.01% Oligonucleotide aptamer	17.5 mL

Table 2 cobas® TV/MG Positive Control Kit

(cobas® TV/MG Positive Control Kit)

Store at 2–8°C

For use on the **cobas®** 5800 System (P/N 09040641190)

For use on the **cobas®** 6800/8800 Systems (P/N 07948689190 or P/N 09040641190)

Kit components	Reagent ingredients	Quantity per kit
TV/MG Positive Control (TV/MG (+) C)	Tris buffer, < 0.05% Sodium azide, < 0.005% EDTA, < 0.003% Poly rA, <0.01% Non-infectious plasmid DNA (microbial) containing *T. vaginalis*, <0.01% Non-infectious plasmid DNA (microbial) containing *M. genitalium*	16 mL (16 x 1 mL)

Table 3 cobas® Buffer Negative Control Kit

(cobas® Buffer Negative Control Kit)

Store at 2-8°C

For use on the **cobas**® 5800 System (P/N 09051953190)

For use on the **cobas**® 6800/8800 Systems (P/N 07002238190 or P/N 09051953190)

Kit components	Reagent ingredients	Quantity per kit
cobas® Buffer Negative Control (BUF (-) C)	Tris buffer, < 0.1% sodium azide, EDTA, < 0.002% Poly rA RNA (synthetic)	16 mL (16 x 1 mL)

cobas® omni reagents for sample preparation

Table 4 **cobas® omni** reagents for sample preparation*

Reagents	Reagent ingredients	Quantity per kit	Safety symbol and warning**
cobas® omni MGP Reagent (MGP) Store at 2–8°C (P/N 06997546190)	Magnetic glass particles, Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide	480 tests	Not applicable
cobas® omni Specimen Diluent (SPEC DIL) Store at 2–8°C (P/N 06997511190)	Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide	4 x 875 mL	Not applicable
cobas® omni Lysis Reagent (LYS) Store at 2–8°C (P/N 06997538190)	43% (w/w) guanidine thiocyanate***, 5% (w/v) polydocanol***, 2% (w/v) dithiothreitol***, dihydro sodium citrate	4 x 875 mL	 **DANGER** H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H412: Harmful to aquatic life with long lasting effects. EUH032: Contact with acids liberates very toxic gas. EUH071: Corrosive to the respiratory tract. P273: Avoid release to the environment. P280: Wear protective gloves/protective clothing/eye protection/face protection/ hearing protection. P301 + P330 + P331: IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor. P305 + P351 + P338 + P310: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/doctor. 593-84-0 Guanidinium thiocyanate 9002-92-0 Polidocanol 3483-12-3 (R*,R*)-1,4-dimercaptobutane-2,3-diol
cobas® omni Wash Reagent (WASH) Store at 15–30°C (P/N 06997503190)	Sodium citrate dihydrate, 0.1% methyl-4 hydroxybenzoate	4.2 L	Not applicable

* These reagents are not included in the **cobas**® TV/MG kit. See listing of additional materials required for **cobas**® 5800 and **cobas**® 6800/8800 (Table 8 and Table 9).

** Product safety labeling primarily follows EU GHS guidance

***Hazardous substance

Reagent storage and handling requirements

Reagents shall be stored and will be handled as specified in Table 5, Table 6 and Table 7.

When reagents are not loaded on the **cobas**® 5800 System or **cobas**® 6800/8800 Systems, store them at the corresponding temperature specified in Table 5.

Table 5 Reagent storage (when reagent is not on the system)

Reagent	Storage temperature
cobas® TV/MG	2–8°C
cobas® TV/MG Positive Control Kit	2–8°C
cobas® Buffer Negative Control Kit	2–8°C
cobas® **omni** Lysis Reagent	2–8°C
cobas® **omni** MGP Reagent	2–8°C
cobas® **omni** Specimen Diluent	2–8°C
cobas® **omni** Wash Reagent	15–30°C

Reagent handling requirements for cobas® 5800 System

Reagents loaded onto the **cobas**® 5800 System are stored at appropriate temperatures and their expiration is monitored by the system. The **s**ystem allows reagents to be used only if all of the conditions shown in Table 6 are met. The system automatically prevents use of expired reagents. Table 6 allows the user to understand the reagent handling conditions enforced by the **cobas**® 5800 System.

Table 6 Reagent expiry conditions enforced by the **cobas**® 5800 System

Reagent	Kit expiration date	Open-kit stability*	Number of runs for which this kit can be used	On-board stability
cobas® TV/MG	Date not passed	90 days from first usage	Max 40 runs	Max 36 days*
cobas® TV/MG Positive Control Kit	Date not passed	Not applicable**	Not applicable	Max 36 days*
cobas® Buffer Negative Control Kit	Date not passed	Not applicable**	Not applicable	Max 36 days*
cobas® **omni** Lysis Reagent	Date not passed	30 days from loading*	Not applicable	Not applicable
cobas® **omni** MGP Reagent	Date not passed	30 days from loading*	Not applicable	Not applicable
cobas® **omni** Specimen Diluent	Date not passed	30 days from loading*	Not applicable	Not applicable
cobas® **omni** Wash Reagent	Date not passed	30 days from loading*	Not applicable	Not applicable

* Time is measured from the first time that reagent is loaded onto the **cobas**® 5800 System.

**Single use reagents

Reagent handling requirements for cobas® 6800/8800 Systems

Reagents loaded onto the **cobas**® 6800/8800 Systems are stored at appropriate temperatures and their expiration is monitored by the system. The **cobas**® 6800/8800 Systems allow reagents to be used only if all of the conditions shown in Table 7 are met. The system automatically prevents use of expired reagents. Table 7 allows the user to understand the reagent handling conditions enforced by the **cobas**® 6800/8800 Systems.

Table 7 Reagent expiry conditions enforced by the **cobas**® 6800/8800 Systems

Reagent	Kit expiration date	Open-kit stability*	Number of runs for which this kit can be used	On-board stability (cumulative time on board outside refrigerator)
cobas® TV/MG	Date not passed	90 days from first usage	Max 40 runs	Max 40 hours
cobas® TV/MG Positive Control Kit	Date not passed	Not applicable**	Not applicable	Max 10 hours
cobas® Buffer Negative Control Kit	Date not passed	Not applicable**	Not applicable	Max 10 hours
cobas® **omni** Lysis Reagent	Date not passed	30 days from loading*	Not applicable	Not applicable
cobas® **omni** MGP Reagent	Date not passed	30 days from loading*	Not applicable	Not applicable
cobas® **omni** Specimen Diluent	Date not passed	30 days from loading*	Not applicable	Not applicable
cobas® **omni** Wash Reagent	Date not passed	30 days from loading*	Not applicable	Not applicable

* Time is measured from the first time that reagent is loaded onto the **cobas**® 6800/8800 Systems.

**Single use reagents

Additional materials required for cobas® 5800 System

Table 8 Material and consumables for use on **cobas**® 5800 System

Material	**P/N**
cobas® **omni** Processing Plate 24	08413975001
cobas® **omni** Liquid Waste Plate 24	08413983001
cobas® **omni** Amplification Plate 24	08499853001
Tip CORE TIPS with Filter, 1ml	04639642001
Tip CORE TIPS with Filter, 300µL	07345607001
cobas® **omni** Liquid Waste Container	07094388001
cobas® **omni** Lysis Reagent	06997538190
cobas® **omni** MGP Reagent	06997546190
cobas® **omni** Specimen Diluent	06997511190
cobas® **omni** Wash Reagent	06997503190
Solid Waste Bag or Solid Waste Bag With Insert	07435967001 or 08030073001
16-position tube S-carrier complete	09224319001
5-position Rack Carrier	09224475001
Cell Collection Media Carrier	09224599001

Additional materials required for cobas® 6800/8800 Systems

Table 9 Materials and consumables for use on **cobas**® 6800/8800 Systems

Material	P/N
cobas® **omni** Processing Plate	05534917001
cobas® **omni** Amplification Plate	05534941001
cobas® **omni** Pipette Tips	05534925001
cobas® **omni** Liquid Waste Container	07094388001
cobas® **omni** Lysis Reagent	06997538190
cobas® **omni** MGP Reagent	06997546190
cobas® **omni** Specimen Diluent	06997511190
cobas® **omni** Wash Reagent	06997503190
Solid Waste Bag and Solid Waste Container or Solid Waste Bag With Insert and Kit Drawer	07435967001 and 07094361001 or 08030073001 and 08387281001
STD-Rack. re-run R001-R025 PINK	12025639001

Instrumentation and software required

The **cobas**® 5800 software and **cobas**® TV/MG analysis package (ASAP) for **cobas**® 5800 shall be installed on the **cobas**® 5800 instrument(s). The Data Manager software and PC for **cobas**® 5800 System will be provided with the system.

The **cobas**® 6800/8800 software and **cobas**® TV/MG analysis package (ASAPs) for **cobas**® 6800/8800 shall be installed on the instrument(s). The Instrument Gateway (IG) server will be provided with the system.

Table 10 Instrumentation

Equipment	P/N
cobas® 5800 System	08707464001
cobas® 6800 System (Option Moveable)	05524245001 and 06379672001
cobas® 6800 System (Fix)	05524245001 and 06379664001
cobas® 8800 System	05412722001
Sample Supply Module for **cobas**® 6800/8800 Systems	06301037001

Additional materials required for sample collection for cobas® TV/MG

Table 11 Specimen collection kits used with **cobas**® TV/MG

Collection Kit	P/N
cobas® PCR Media Kit	06466281190
cobas® PCR Urine Sample Kit	05170486190
cobas® PCR Media Uni Swab Sample Kit	07958030190
cobas® PCR Media Dual Swab Sample Kit	07958021190
ThinPrep Pap Test Physician's Kit (500 vials & Broom-like collection devices) ThinPrep Pap Test Physician's Kit (500 vials & Cytobrush/spatula collection devices)	Hologic: 70136-001 Hologic: 70136-002

cobas® TV/MG accepts the primary tube used for all **cobas**® PCR media swab and urine specimen types. Refer to the **cobas**® 5800 System or the **cobas**® 6800/8800 Systems User Assistance and/or User Guides for additional information for primary and secondary sample tubes accepted on the instruments.
Note: Contact your local Roche representative for a detailed order list for sample racks, racks for clotted tips and rack trays accepted on the instruments

Additional materials required for sample aliquoting and sample loading for cobas® TV/MG

Table 12 Specimen collection kits used with **cobas**® TV/MG

Material	P/N
cobas® PCR Media Secondary Tube Kit	07958048190
cobas® PCR Media Tube Replacement Cap Kit	07958056190
Replacement Caps for PreservCyt® Vials	08037230190
cobas® PCR Media Disposable Tube Stand (Optional)	07958064190
MPA RACK 16 MM LIGHT GREEN 7001-7050[a,b,c]	03143449001
RD5 RACK – RD Standard rack 0001-0050 LR[a,b,c]	11902997001

[a] RD5 or MPA racks are required in combination with the 5-position Rack Carrier on the **cobas**® 5800 System.

[b] MPA 16mm rack or 16-position tube carrier are the preferred racks for use with samples collected in **cobas**® PCR Media tubes.

[c] MPA and RD5 racks identified here are example materials and part numbers. Please contact your local Roche representative for a detailed order list for sample racks and rack carriers accepted on the instruments.

Precautions and handling requirements

Warnings and precautions

As with any test procedure, good laboratory practice is essential to the proper performance of this assay. Due to the high sensitivity of this test, care should be taken to keep reagents and amplification mixtures free of contamination.

- For in vitro diagnostic use only.
- All patient samples should be handled as if infectious, using good laboratory procedures as outlined in Biosafety in Microbiological and Biomedical Laboratories and in the CLSI Document M29-A4.[18,19] Only personnel proficient in handling infectious materials and the use of **cobas**® TV/MG and **cobas**® 5800 System or **cobas**® 6800/8800 Systems should perform this procedure.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions. If spillage occurs, immediately disinfect with a freshly prepared solution of 0.6% sodium or potassium hypochlorite in distilled or deionized water or follow appropriate site procedures.
- Do not freeze any samples.
- Use only supplied or specified required consumables to ensure established test performance.
- Safety Data Sheets (SDS) are available on request from your local Roche representative.
- Closely follow procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect established test performance.
- False positive results may occur if carryover of samples is not adequately controlled during sample handling and processing.
- **cobas**® PCR Media (from primary specimen tube) contains guanidine hydrochloride. **Do not allow direct contact between guanidine hydrochloride and sodium hypochlorite (bleach) or other highly reactive reagents such as acids or bases. These mixtures can release a noxious gas**. If liquid containing guanidine hydrochloride is spilled, clean with suitable laboratory detergent and water. If the spilled liquid contains potentially infectious agents, **FIRST** clean the affected area with laboratory detergent and water, and then with at least 0.5% sodium hypochlorite.
- Inform your local competent authority about any serious incidents which may occur when using this assay.

Reagent handling

- Handle all reagents, controls, and samples according to good laboratory practice in order to prevent carryover of samples, reagents, or controls.
- Before use, visually inspect each reagent cassette, diluent, lysis reagent, and wash reagent to ensure that there are no signs of leakage. If there is any evidence of leakage, do not use that material for testing.
- **cobas**® **omni** Lysis Reagent contains guanidine thiocyanate, a potentially hazardous chemical. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur.
- Do not allow **cobas**® **omni** Lysis Reagent, which contains guanidine thiocyanate, to contact sodium hypochlorite (bleach) solution. This mixture can produce a highly toxic gas.
- Expended control kits contain pierced vials with residual reagent; special care should be taken during disposal to avoid spills and contact.
- **cobas**® TV/MG kit, **cobas**® TV/MG Positive Control kit, **cobas**® Buffer Negative Control kit, **cobas**® **omni** MGP Reagent, and **cobas**® **omni** Specimen Diluent contain sodium azide as a preservative. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur. If these reagents are spilled, dilute with water before wiping dry.
- Do not allow **cobas**® **omni** Lysis Reagent, which contains guanidine thiocyanate, to contact sodium hypochlorite (bleach) solution. This mixture can produce a highly toxic gas.
- Dispose of all materials that have come in contact with samples and reagents in accordance with country, state, and local regulations.

Good laboratory practice

- Do not pipette by mouth.
- Do not eat, drink, or smoke in designated work areas.
- Wear laboratory gloves, laboratory coats, and eye protection when handling samples and reagents. Avoid contaminating gloves when handling samples and controls. Gloves must be changed between handling samples and **cobas**® TV/MG kit, **cobas**® TV/MG Positive Control kit, **cobas**® Buffer Negative Control kit**,** and **cobas**® **omni** reagents to prevent contamination.
- Wash hands thoroughly after handling samples and reagents, and after removing the gloves.
- Thoroughly clean and disinfect all laboratory work surfaces with a freshly prepared solution of 0.6% sodium or potassium hypochlorite in distilled or deionized water. Follow by wiping the surface with 70% ethanol.
- If spills occur on the **cobas**® 5800 instrument or **cobas**® 6800/8800 instruments, follow the instructions in the **cobas**® 5800 System or **cobas**® 6800/8800 Systems User Assistance and/or User Guides to properly clean and decontaminate the surface of instrument(s).

Specimen collection, transport, and storage

Note: Handle all samples and controls as if they are capable of transmitting infectious agents.

Specimen collection

Endocervical swab specimens collected with the **cobas**® PCR Media Dual Swab Sample Kit, vaginal swab specimens and meatal swab specimens collected with either the **cobas**® PCR Media Uni Swab Sample Kit or **cobas**® PCR Media Dual Swab Sample Kit, male and female urine collected with the **cobas**® PCR Urine Sample Kit and cervical specimens collected in PreservCyt® Solution may be used with **cobas**® TV/MG (see Table 11 for a list of all collection kits). Follow the instructions for collecting all swab and urine specimens in their respective collection kit IFU. Follow the manufacturer's instructions for collecting cervical specimens into PreservCyt® Solution.

Specimen transport

All specimen types listed in Specimen Collection section can be transported at 2-30°C. Transportation of TV/MG specimens in **cobas**® PCR Media and PreservCyt® Solution must comply with country, federal, state and local regulations for the transport of etiologic agents.[20]

Specimen storage

Table 13 Summary of acceptable specimen storage conditions prior to testing with **cobas**® TV/MG

Specimen Type		2-8°C	15-30°C
Samples in **cobas**® PCR Media		12 months	12 months
PreservCyt®	in collection device	90 days	90 days
	or		
	PreservCyt® aliquoted to secondary tubes	31 days	31 days

Note: PreservCyt® and **cobas**® PCR Media specimens should not be frozen.

Male and female urine specimens

- Use only the **cobas**® PCR Urine Sample Kit to collect urine specimens for **cobas**® TV/MG. **cobas**® TV/MG has not been validated for use with other urine collection devices or media types. Using **cobas**® TV/MG with other urine collection devices or other media types may lead to false negative, false positive, and/or invalid results.
- To avoid cross contamination of processed specimens, additional caps for **cobas**® PCR Media tubes in an alternate color (neutral; see **Additional materials required for sample aliquoting and sample loading for cobas® TV/MG**) should be used to recap specimens after processing.
- Untested urine specimens must show the top of the liquid level between the two black lines on the **cobas**® PCR Media tube label window. If the liquid level is above or below these lines, the specimen has not been collected properly and cannot be used for testing.
- If additional testing is required, ensure that there is at least 1.2 mL of specimen remaining the in **cobas**® PCR Media tube.

Endocervical and vaginal specimens

- The presence of mucus in endocervical and cervical specimens may cause processing delays due to clotting. Mucus free specimens are required for optimal test performance. Use the large woven polyester swab in the **cobas**® PCR Media Dual Swab Sample Kit or an equivalent device to remove cervical secretions and discharge before obtaining the endocervical or cervical specimen.
- Use only the flocked swab in the **cobas**® PCR Media Dual Swab Sample Kit to collect endocervical specimens. Use only the woven polyester swab in either the **cobas**® PCR Media Uni Swab Sample Kit or the **cobas**® PCR Media Dual Swab Sample Kit to collect vaginal swab specimens. **cobas**® TV/MG has not been validated for use with other swab collection devices or media types. Using **cobas**® TV/MG with other swab collection devices or media types may lead to false negative, false positive, and/or invalid results.
- To avoid cross contamination of processed specimens, additional caps for **cobas**® PCR Media tubes in an alternate color (neutral; see **Additional materials required for sample aliquoting and sample loading for cobas® TV/MG**) should be used to recap specimens after processing.
- All swab specimens containing a single swab in the **cobas**® PCR Media tube can be directly processed on the **cobas**® 5800 or **cobas**® 6800/8800 Systems. If desired, the swab may be removed before the specimen tube is loaded onto the instrument, however utmost care must be exercised to avoid cross contamination.
- A properly collected swab specimen should have a single swab with the shaft broken at the scoreline. Swab shafts which are broken above the score line will appear longer than normal and may also be bent over to fit into the **cobas**® PCR Media tube. This can create an obstruction to the pipetting system which may cause the loss of sample, test results and/or mechanical damage to the instrument. In the event that a swab specimen has an improperly broken shaft, remove the swab prior to sample processing on the **cobas**® 5800 or **cobas**® 6800/8800 Systems. Use caution when disposing of specimen swabs; avoid splashing or touching swabs to other surfaces during disposal to prevent contamination.
- Incoming primary swab specimen tubes with no swabs or with two swabs have not been collected according to the instructions in their respective collective kit IFU and should not be tested.
- Occasionally, incoming swab specimens contain excessive mucus which may induce a pipetting error (e.g., clot or other obstruction) on the **cobas**® 5800 or **cobas**® 6800/8800 Systems. Prior to retesting of specimens that exhibited clots during initial processing, remove and discard the swab, then re-cap and vortex these specimens for 30 seconds to disperse the excess mucus.
- Swab specimens can be assayed twice on the **cobas**® 5800 or **cobas**® 6800/8800 Systems while the swab is in the collection tube. If additional testing is required, or if the first test fails due to specimen pipetting error (e.g., clot or other obstruction), the swab must be removed and the remaining fluid must have a minimum volume of 1.0 mL.

Meatal specimens

- Use only the woven polyester swab in either the **cobas**® PCR Media Uni Swab Sample Kit or the **cobas**® PCR Media Dual Swab Sample Kit to collect meatal swab specimens. cobas® TV/MG is validated for use with meatal swab specimens collected in cobas® PCR Media for the detection of M. genitalium. **cobas**® TV/MG has not been validated for use with other swab collection devices or media types. Using **cobas**® TV/MG with other swab collection devices or media types may lead to false negative, false positive, and/or invalid results.
- To avoid cross contamination of processed specimens, additional caps for **cobas**® PCR Media tubes in an

alternate color (neutral; see **Additional materials required for sample aliquoting and sample loading for cobas® TV/MG**) should be used to recap specimens after processing.

- All meatal swab specimens containing a single swab in the **cobas**® PCR Media tube can be directly processed on the **cobas**® 5800 or **cobas**® 6800/8800 Systems while the volume in the collection tube is greater than 1.5 mL. If desired, the swab may be removed before the specimen tube is loaded onto the instrument, however utmost care must be exercised to avoid cross contamination.
- A properly collected swab specimen should have a single swab with the shaft broken at the scoreline. Swab shafts which are broken above the score line will appear longer than normal and may also be bent over to fit into the **cobas**® PCR Media tube. This can create an obstruction to the pipetting system which may cause the loss of sample, test results and/or mechanical damage to the instrument. In the event that a swab specimen has an improperly broken shaft, remove the swab prior to sample processing on the **cobas**® 5800 or **cobas**® 6800/8800 Systems. Use caution when disposing of specimen swabs; avoid splashing or touching swabs to other surfaces during disposal to prevent contamination.
- Incoming primary swab specimen tubes with no swabs or with two swabs have not been collected according to the instructions in their respective collective kit IFU and should not be tested.
- Meatal Swab specimens can be assayed twice on the **cobas**® 5800 or **cobas**® 6800/8800 Systems while the swab is in the collection tube. If additional testing is required, or if the first test fails due to specimen pipetting error (e.g., clot or other obstruction), the swab must be removed and the remaining fluid must have a minimum volume of 1.2 mL.

Cervical specimens in PreservCyt® Solution

cobas® TV/MG is validated for use with cervical specimens collected in PreservCyt® Solution for the detection of T. vaginalis prior to cytology processing. **cobas**® TV/MG has not been validated for use with cervical specimens obtained in other media types. Using **cobas**® TV/MG with other media types may lead to false negative, false positive, and/or invalid results.

cobas® 5800 System

- The **cobas**® 5800 System may process cervical specimens in PreservCyt® Solution directly out of their primary containers with a proper barcode or out of a properly barcoded **cobas**® PCR Media Secondary Tube (see **cobas**® 5800/6800/8800 System section below for optional aliquoting instructions for **cobas**® 5800 System).
    1. With clean gloved hands, vortex the capped primary vial for **10 seconds** immediately **prior** to loading.
    2. Uncap the primary vial and place on a Cell Collection Media Carrier
- For primary vial loading, the minimum volume required in the PreservCyt® Solution primary containers is 3.0 mL.

cobas® 5800/6800/8800 Systems

- Cervical specimens in PreservCyt® Solution should be aliquoted into **cobas**® PCR Media Secondary Tubes as follows, for processing on the **cobas**® 5800 System or **cobas**® 6800/8800 Systems:
    1. Prepare a barcoded **cobas**® PCR Media Secondary Tube for each PreservCyt® specimen to be tested.
    2. With clean gloved hands, vortex each PreservCyt® primary specimen vial for 10 seconds immediately prior to transfer.
    3. Uncap a primary vial and transfer at least 1.0 mL but no more than 4.0 mL into the prepared barcoded secondary tube from step 1.
        - *Always use caution when transferring specimens from primary containers to secondary tubes.*
        - *Always use a new pipette tip for each specimen.*
        - *Always use pipettors with aerosol-barrier or positive-displacement tips to handle specimens.*
        - *To avoid cross contamination, additional caps for these tubes in an alternate color (neutral; see **Additional materials required for sample aliquoting and sample loading for cobas® TV/MG**) should be used to recap these specimens after processing.*
        - *Transfer tube to a rack if testing is to be performed shortly after or cap the secondary tube if testing will be performed at a future time.*
    4. Re-cap the primary vial with a replacement cap before moving to the next specimen. Store the primary vial upright.
    5. Only racks of uncapped tubes should be loaded on to the systems for TV/MG testing.
- Aliquots of the primary specimen must contain a minimum volume of 1.0 mL.

Instructions for use

Procedural notes

- Do not use **cobas**® TV/MG, **cobas**® TV/MG Positive Control Kit, **cobas**® Buffer Negative Control Kit, or **cobas**® **omni** reagents after their expiry dates.
- Do not reuse consumables. They are for one-time use only.
- Ensure that specimen barcode labels on sample tubes are visible through the openings on the side of sample carriers. Refer to the **cobas**® 5800 System or **cobas**® 6800/8800 Systems User Assistance and/or User Guides for proper barcode specifications and additional information on loading sample tubes.
- Refer to the **cobas**® 5800 System or **cobas**® 6800/8800 Systems User Assistance and/or User Guides for proper maintenance of instruments.

Running cobas® TV/MG on cobas® 5800 System

cobas® TV/MG can be run with a minimum required sample volume of 1.0 mL for swab and PreservCyt® specimens, 1.2 mL for urine and meatal specimens in **cobas**® PCR Media Tube, and 3.0 mL for PreservCyt® specimens in primary vial. The operation of the instrument is described in detail in the **cobas**® 5800 System User Assistance Guide. Figure 1 below summarizes the procedure.

- Swab and Urine specimens should be uncapped and loaded directly onto racks for processing on the **cobas**® 5800 System.
- PreservCyt® specimens may be uncapped and run from primary vials.
  Note: Use slow and steady movements when loading and unloading the Cell Collection Media Carrier (holding primary vials) to avoid splashing of specimens.
- Optionally, PreservCyt® specimens may be aliquoted into barcoded 13 mL round-bottom **cobas**® PCR Media Secondary tubes for processing on the **cobas**® 5800 System. Refer to the preparation instructions for cervical specimens found in section: “Cervical specimens in PreservCyt® Solution”
- A single run can have any combination of specimens (Swab, Urine, and PreservCyt®) and each specimen can be tested for either TV/MG, TV, or MG.
- Specimens collected in **cobas**® PCR Media or PreservCyt® Solution should be processed using the sample type selection in the user interface (UI) of the **cobas**® TV/MG as described in Table 14.

Table 14 Sample type selection in the user interface of the **cobas**® TV/MG

Specimen		**Collection kit type**	**Process as Sample Type**
Female	Vaginal swab	**cobas**® PCR Media Uni or Dual Swab Sample Kit	**Swab**
	Endocervical swab	**cobas**® PCR Media Dual Swab Sample Kit	**Swab**
	Urine	**cobas**® PCR Urine Sample Kit or **cobas**® PCR Media Kit	**Urine**
	Cervical specimens	PreservCyt® Solution (ThinPrep)	**PreservCyt**®
Male	Urine	**cobas**® PCR Urine Sample Kit or **cobas**® PCR Media Kit	**Urine**
	Meatal swab	**cobas**® PCR Media Uni or Dual Swab Sample Kit	**Meatal Swab***

*For manual and rack-based ordering: Make sure to select “Meatal Swab”, not “Swab”, as the sample type for Meatal Swab specimens. Swab sample type includes only: vaginal and endocervical swab specimens.

Figure 1 **cobas**® TV/MG procedure on **cobas**® 5800 System

1 Log onto the system

2 Loading specimens onto the system

- For each urine or swab in **cobas**® PCR Media
  - Uncap tube
  - Transfer tube directly to rack
- For each primary PreservCyt® specimen vial:
  - If loading primary vial:
    - Vortex for 10 seconds
    - Uncap vial
    - Transfer vial to rack
  - If loading secondary tube:
    - Vortex for 10 seconds
    - Aliquot a minimum of 1 mL of PreservCyt® specimen into a **cobas**® PCR Media Secondary tube
    - Transfer tube to rack
- Load sample rack

Confirm samples have been accepted into the system

Order Tests

- Choose “Swab” for ordering endocervical and vaginal swab specimens collected in **cobas**® PCR Media
- Choose “Urine” for ordering male and female urine specimens collected in **cobas**® PCR Media
- Choose “Meatal Swab” for ordering meatal swab specimens collected in **cobas**® PCR Media
- Choose “PreservCyt” for ordering PreservCyt® Solution (cervical specimens)

Choose the Test name

3 Refill reagents and consumables as prompted by the system

- Load test specific reagent cassette
- Load control mini racks
- Load processing tips
- Load elution tips
- Load processing plates
- Load amplification plates
- Load Liquid waste plates
- Load MGP Reagent

Refill Specimen Diluent

Refill Lysis Reagent

Refill Wash Reagent

4 Start the run by choosing the Start processing button on the user interface, all subsequent runs will start automatically if not manually postponed

5 Review and export results

6 Remove sample tubes. If needed, cap any sample tubes meeting the minimum volume requirements for future use.

Clean up instrument

- Unload empty test specific reagent cassette(s)
- Unload empty control mini racks
- Empty amplification plate drawer
- Empty liquid waste
- Empty solid waste

Running cobas® TV/MG on cobas® 6800/8800 Systems

cobas® TV/MG can be run with a minimum required sample volume of 1.0 mL for endocervical and vaginal swabs and cervical specimens in PreservCyt®, and 1.2 mL for meatal swab and urine specimens. The operation of the instrument is described in detail in the **cobas**® 6800/8800 Systems User Assistance. Figure 2 below summarizes the procedure.

- Female Swab, Urine, and Meatal Swab specimens should be uncapped and can be loaded directly onto racks for processing on the **cobas**® 6800/8800 Systems.
- It is necessary to aliquot cervical specimens collected in PreservCyt® Solution. Refer to the preparation instructions found in the section: "Cervical specimens in PreservCyt® Solution".
- A single run can have any combination of specimens (Swab, Urine, Meatal Swab, and PreservCyt®) and each specimen can be tested with either the TV/MG, TV, or MG ASAPs.
- Specimens collected in **cobas**® PCR Media or PreservCyt® Solution should be processed using the sample type selection in the user interface (UI) of the **cobas**® TV/MG as described in Table 15.

Table 15 Sample type selection in the user interface of the **cobas**® TV/MG

Specimen		**Collection kit type**	**Process as Sample Type**
Female	Vaginal swab	**cobas**® PCR Media Uni or Dual Swab Sample Kit	**Swab**
	Endocervical swab	**cobas**® PCR Media Dual Swab Sample Kit	**Swab**
	Urine	**cobas**® PCR Urine Sample Kit	**Urine**
	Cervical specimens	PreservCyt® Solution (ThinPrep)	**PreservCyt®**
Male	Urine	**cobas**® PCR Urine Sample Kit	**Urine**
	Meatal swab	**cobas**® PCR Media Uni or Dual Swab Sample Kit	**Meatal Swab***

*For manual and rack-based ordering: Make sure to select "Meatal Swab", not "Swab", as the sample type for Meatal Swab specimens.
Swab sample type includes only: vaginal and endocervical swab specimens.

Figure 2 **cobas**® TV/MG procedure on **cobas**® 6800/8800 Systems

1

Log onto the system
Press Start to Prepare the system
Order Tests

- Choose “Swab” for ordering endocervical and vaginal swab specimens collected in **cobas**® PCR Media
- Choose “Urine” for ordering male and female urine specimens collected in **cobas**® PCR Media
- Choose “Meatal Swab” for ordering meatal swab specimens collected in **cobas**® PCR Media
- Choose “PreservCyt” for ordering PreservCyt® Solution (cervical specimens)
- Choose the Test

2

Refill reagents and consumables as prompted by the system

- Load test specific reagent cassette
- Load control cassettes
- Load Pipette Tips
- Load Processing Plates
- Load MGP Reagent
- Load Amplification Plates
- Refill Specimen Diluent
- Refill Lysis Reagent
- Refill Wash Reagent

3

Loading specimens onto the system

- For each primary Urine, Swab, or Meatal Swab in **cobas**® PCR Media
  - Uncap tube
  - Transfer tube directly to rack
- For each primary PreservCyt® specimen vial:
  - Vortex for 10 seconds
  - Aliquot a minimum of 1 mL of PreservCyt® specimen into a 13 mL round-bottom secondary tube
  - Transfer tube to rack
- Load sample rack and clot tip racks into the sample supply module
- Confirm samples have been accepted into the transfer module

4

Start run

5

Review and export results

6

Remove and cap any sample tubes meeting the minimum volume requirements if needed for future use

Clean up instrument

- Unload empty control cassettes
- Empty amplification plate drawer
- Empty liquid waste
- Empty solid waste

Results

The **cobas**® 5800 System and **cobas**® 6800/8800 Systems automatically detects and discriminates TV and/or MG DNA simultaneously for samples and controls, displaying test validity, overall results, as well as individual target results.

Quality control and validity of results on the cobas® 5800 System

- One **cobas**® Buffer Negative Control [(-) Ctrl] and one TV/MG Positive Control [TV/MG (+) C] must be processed at least every 72 hours or with every new kit lot. Positive and/or negative controls can be scheduled more frequently based on laboratory procedures and/or local regulations.
- The results of the controls are shown in the **cobas**® 5800 software in the "Controls" app.
- In the **cobas**® 5800 System software and/or report, check for flags to ensure the validity of the corresponding test results (Refer to the x800 Data Manager User Assistance for a 'List of flag codes').
- The controls are valid if no flags appear for either control.
- Controls are marked with "Valid" in the column "Control result" if all Targets of the control are reported valid. Controls are marked with 'Invalid' in the column "Control result" if one or both Targets of the control are reported invalid.
- Controls marked with 'Invalid' show a flag in the "Flags" column. More information on why the control is reported invalid including flag information will be shown in the detail view. If the positive control is invalid, repeat testing the positive control and all associated samples. If the negative control is invalid, repeat testing all controls and all associated samples.

Invalidation of results is performed automatically by the **cobas**® 5800 software based on control results.

NOTE: The **cobas**® 5800 System will be delivered with the standard setting of running a set of controls (positive and negative) with every run, but can be configured to a less frequent scheduling up to every 72 hours based on laboratory procedures and/or local regulations. Please contact your Roche service engineer and/or Roche customer technical support for more information.

Quality control and validity of results on the cobas® 6800/8800 Systems

- One **cobas**® Buffer Negative Control [(-) Ctrl] and one TV/MG Positive Control [TV/MG (+) C] are processed with each batch of a requested result type.
- In the **cobas**® 6800/8800 software and/or report, check for flags and their associated results to ensure batch validity.
- All flags are described in the **cobas**® 6800/8800 Systems User Assistance.
- The batch is valid if no flags appear for all controls. If the batch is invalid, repeat testing of the entire batch.

Validation of results is performed automatically by the **cobas**® 6800/8800 software based on negative and positive control performance.

cobas® TV/MG for cobas® 5800 System

The results of the samples are shown in the **cobas**® 5800 software in the "Results" app. Display examples for **cobas**® TV/MG for **cobas**® 5800 System Software are shown in Figure 3.

Figure 3 Example of **cobas**® TV/MG results display for **cobas**® 5800 System

Sample ID*	Test	Control results	Flag**	Result
TV/MG_01	TV/MG	Valid		**TV Negative MG Negative**
MG 01_	MG	Valid		**MG Positive (Ct 36.52)**
TV/MG_02	TV/MG	Valid		**TV Invalid MG Invalid**
TV 01	TV	Valid		**TV Negative**
TV/MG_03	TV/MG	Valid		**TV Positive (Ct 35.44) MG positive (Ct 36.00)**

* Table applies for all sample types used.

** The result overview shows a flag symbol in case of invalid results. Detailed flag descriptions are available in the result details.

Check each individual sample for flags in the **cobas**® 5800 System software and/or report. The result interpretation should be as follows:

- Samples associated with valid controls are shown as 'Valid' in the "Control result" column.
- Samples associated with a failed control are shown as 'Invalid' in the "Control result" column.
- If the associated controls of a sample result are invalid, a specific flag will be added to the sample result as follows:
    - Q05D : Result validation failure because of an invalid positive control
    - Q06D :Result validation failure because of an invalid negative control
- The values in "Results" column for individual sample target result should be interpreted as shown in Figure 4, Figure 5 and Figure 6 below.
- If one or more sample targets are marked with "Invalid" the **cobas**® 5800 software shows a flag in the "Flags" column. More information on why the sample target(s) is reported invalid including flag information is shown in the detail view.
- Invalid results for one or more target combinations are possible with the TV/MG result request and are reported out specifically for each channel. Refer to retesting instructions for the respective specimen type.
- Results of this test should only be interpreted in conjunction with information available from clinical evaluation of the patient and patient history.

cobas® TV/MG for cobas® 6800/8800 Systems

Display examples for **cobas**® TV/MG for **cobas**® 6800/8800 Systems are shown in Figure 4, Figure 5, and Figure 6, respectively.

Figure 4 Example of **cobas**® TV/MG results display for TV/MG result request for **cobas**® 6800/8800 Systems

Test	Sample ID	Valid	Flags	Sample type	Overall result	Target 1	Target 2
TV/MG 850 µL	UR_TVMGNegPos_B1	NA		Urine	**NA**	TV Negative	MG Positive
TV/MG 850 µL	UR_TVMGPos_B2	NA		Urine	**NA**	TV Positive	MG Positive
TV/MG 400 µL	SB_TVMGPosInv_01	NA	C01H2	Swab	**NA**	TV Positive	Invalid
TV/MG 400 µL	SB_TVMGInvPos_A2	NA	C01H1	Swab	**NA**	Invalid	MG Positive
TV/MG	C161420284090428828404	Yes		(-) Ctrl	**Valid**	Valid	Valid
TV/MG	C161420284093009580264	Yes		TV/MG (+) C	**Valid**	Valid	Valid

Figure 5 Example of **cobas**® TV results display for TV result request for **cobas**® 6800/8800 Systems

Test	Sample ID	Valid	Flags	Sample type	Overall result	Target 1	Target 2
TV 400 µL	SB_TVInv_01	NA	Y40T	Swab	**NA**	Invalid	
TV 400 µL	SB_TVNeg_01	NA		Swab	**NA**	TV Negative	
TV 850 µL	UR_TVPos_A5	NA		Urine	**NA**	TV Positive	
TV 850 µL	UR_TVNeg_01	NA		Urine	**NA**	TV Negative	
TV 850 µL	PC_TVPos_A3	NA		PreservCyt®	**NA**	TV Positive	
TV 850 µL	PC_TVNeg_01	NA		PreservCyt®	**NA**	TV Negative	
TV	C161420284093009580263	Yes		TV/MG (+) C	**Valid**	Valid	
TV	C161420284090428828403	Yes		(-) Ctrl	**Valid**	Valid	

Note: No results are shown under Target 2 because it is reserved for MG results.

Figure 6 Example of **cobas**® MG results display for MG result request for **cobas**® 6800/8800 Systems

Test	Sample ID	Valid	Flags	Sample type	Overall result	Target 1	Target 2
MG 850 µL	UR_ MGVNeg_A1	NA		Urine	**NA**		MG Negative
MG 850 µL	UR_MGNeg_01	NA		Urine	**NA**		MG Negative
MG 850 µL	MS_MGInv_01	NA	Y40T	Meatal Swab	**NA**		Invalid
MG 850 µL	MS_MGPos_A2	NA		Meatal Swab	**NA**		MG Positive
MG 400 µL	SB_MGPos_A7	NA		Swab	**NA**		MG Positive
MG 400 µL	SB_MGNeg_01	NA		Swab	**NA**		MG Negative
MG	C16142028409300950734	Yes		TV/MG (+) C	**Valid**		Valid
MG	C161420284090428828402	Yes		(-) Ctrl	**Valid**		Valid

Note: No results are shown under Target 1 because it is reserved for TV results.

For a valid batch, check each individual sample for flags in the **cobas**® 6800/8800 software and/or report. The result interpretation should be as follows:

- A valid batch may include both valid and invalid sample results.
- The "Valid" and "Overall Result" columns are not applicable (NA) to sample results for the **cobas**® TV/MG and are marked with "NA". Values reported in these columns are not applicable and **do not** impact the validity of results reported within individual Target Result columns.
- Reported target results for individual samples are valid unless indicated as "Invalid" within the individual target result column.
- Invalid results for one or more target combinations are possible with the TV/MG result request and are reported out specifically for each channel. Refer to the retesting instructions for respective specimen type.
- Results of this test should only be interpreted in conjunction with information available from clinical evaluation of the patient and patient history.

Interpretation of results

Results and their corresponding interpretation for detecting TV and MG (Table 16), TV only (Table 17) and MG only (Table 18) are shown below.

Table 16 cobas® TV/MG results and interpretation for the TV/MG result request

Result		Interpretation
TV Positive	MG Positive	All requested results were valid. Target signal detected for TV and MG DNA.
TV Positive	MG Negative	All requested results were valid. Target signal detected for TV DNA. No target signal detected for MG DNA.
TV Negative	MG Positive	All requested results were valid. No target signal detected for TV DNA. Target signal detected for MG DNA.
TV Negative	MG Negative	All requested results were valid. No target signal detected for TV or MG DNA.
TV Positive	Invalid	Not all requested results were valid. Target signal detected for TV DNA. TV result is valid. MG result is invalid. Original specimen should be re-tested to obtain valid MG results. If the result is still invalid, a new specimen should be obtained.

Result		Interpretation
Invalid	MG Positive	Not all requested results were valid. TV result is invalid. Original specimen should be re-tested to obtain valid TV results. If the result is still invalid, a new specimen should be obtained. Target signal detected for MG DNA. MG result is valid.
TV Negative	Invalid	Not all requested results were valid. No target signal detected for TV DNA. TV result is valid. MG result is invalid. Original specimen should be re-tested to obtain valid MG results. If the result is still invalid, a new specimen should be obtained.
Invalid	MG Negative	Not all requested results were valid. TV result is invalid. Original specimen should be re-tested to obtain valid TV results. If the result is still invalid, a new specimen should be obtained. No target signal detected for MG DNA. MG result is valid.
Invalid	Invalid	Both TV and MG results are invalid. Original specimen should be re-tested to obtain valid TV and MG results. If the results are still invalid, a new specimen should be obtained.

Table 17 cobas® TV/MG results and interpretation for the TV result request

Result	Interpretation
TV Positive	The requested result was valid. Target signal detected for TV DNA.
TV Negative	The requested result was valid. No target signal detected for TV DNA
Invalid	TV result is invalid. Original specimen should be re-tested to obtain valid TV results. If the result is still invalid, a new specimen should be obtained.

Table 18 cobas® TV/MG results and interpretation for the MG result request

Result	Interpretation
MG Positive	The requested result was valid. Target signal detected for MG DNA.
MG Negative	The requested result was valid. No target signal detected for MG DNA
Invalid	MG result is invalid. Original specimen should be re-tested to obtain valid MG results. If the result is still invalid, a new specimen should be obtained.

Procedural limitations

- Use of this product must be limited to personnel trained in the techniques of PCR and the use of the **cobas**® 5800 System or **cobas**® 6800/8800 Systems.
- **cobas**® TV/MG has been evaluated only for use in combination with the **cobas**® TV/MG Positive Control Kit, **cobas**® Buffer Negative Control Kit, **cobas**® **omni** MGP Reagent, **cobas**® **omni** Lysis Reagent, **cobas**® **omni** Specimen Diluent, and **cobas**® **omni** Wash Reagent for use on the **cobas**® 5800 System or **cobas**® 6800/8800 Systems.
- Reliable results depend on proper sample collection, storage and handling procedures.
- Products containing carbomer(s), including vaginal lubricants, creams and gels may interfere with the test and should not be used during or prior to collecting urogenital specimens. See Interference results (Table 23) for further details.
- **cobas**® TV/MG has been validated for the detection of TV and MG DNA in male and female urine, clinician-instructed self-collected vaginal swab specimens, clinician-collected vaginal swab specimens and endocervical specimens, all collected in **cobas**® PCR Media (Roche Molecular Systems, Inc.). cobas® TV/MG has been validated for the detection of TV DNA from cervical specimens collected in PreservCyt® Solution and for the detection of MG DNA from clinician-instructed self-collected meatal swab specimens, and clinician-collected meatal swab specimens, collected in **cobas**® PCR Media (Roche Molecular Systems, Inc.). Assay performance has not been established with other collection media and/or specimen types.
- **cobas**® TV/MG has not been evaluated in patients younger than 14 years of age.
- Detection of *T. vaginalis* and *M. genitalium* is dependent on the number of organisms present in the specimen and may be affected by specimen collection methods, patient factors (i.e., age, history of STD, presence of symptoms), stage of infection and/or infecting *T. vaginalis* and *M. genitalium* strains.
- **cobas**® TV/MG for urine testing is recommended to be performed on first catch urine specimens (defined as the first 10 to 50 mL of the urine stream). The effects of other variables such as first-catch vs. mid-stream, post-douching, etc. have not been evaluated.
- The effects of other potential variables such as vaginal discharge, use of tampons, douching, etc. and specimen collection variables have not been evaluated.
- **cobas**® TV/MG has not been evaluated with patients who were currently being treated with antimicrobial agents active against TV or MG as well as patients with a history of hysterectomy.
- False negative or invalid results may occur due to polymerase inhibition. The Internal Control is included in **cobas**® TV/MG to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- The addition of AmpErase enzyme into the **cobas**® TV/MG Master Mix reagent enables selective amplification of target DNA; however, good laboratory practices and careful adherence to the procedures specified in this Instructions-For-Use document are necessary to avoid contamination of reagents.
- Though rare, mutations within the highly conserved regions of the genomic DNA of *T. vaginalis* or the genomic DNA of *M. genitalium* covered by **cobas**® TV/MG primers and/or probes may result in failure to detect the presence of the bacterium.
- Due to inherent differences between technologies, it is recommended that, prior to switching from one technology to the next; users perform method correlation studies in their laboratory to qualify technology differences.

Non-clinical performance evaluation

Key performance characteristics performed on the cobas® 6800/8800 Systems

Limit of Detection (LoD)

The limit of detection of **cobas**® TV/MG was determined by analysis of serial dilutions of two TV (RP - metronidazole susceptible and CDC085 - metronidazole resistant) and two different (MG37 and M30) MG strains. Panels of six to seven concentration levels plus a blank were tested over three lots of **cobas**® TV/MG test reagents, multiple runs, days, operators, and instruments.

The LoD for TV ranged from 0.02 cells/mL (TV strain CDC085 in urine) to 0.16 cells/mL (RP strain in vaginal swab).

The LoD for MG ranged from 0.3 cp/mL (MG strain G37 in urine) to 3.2 cp/mL (MG strain M30 in vaginal swab).

Inclusivity

The inclusivity of **cobas**® TV/MG was confirmed by testing eight TV *(C-1:NIH, 123414, 129155-8, CDC337, NYH 209, PRA-98, 801805, BACT-053LR01)* and five MG (SEA-1, M2288, M2300, M2321, M2341) strains. All TV strains were detected at or below 0.16 cells/mL and all MG strains at or below 3.2 cp/mL.

Precision

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 equivalent to vaginal and meatal swab specimens collected in **cobas**® PCR Media or in cervical specimens collected in PreservCyt® Solution. Sources of variability were examined with a panel consisting of four concentration levels, using three lots of **cobas**® TV/MG reagents and two instruments over a time course of 12 days and with a total of 24 runs. A description of the precision panels and the study performance positivity rates are shown in Table 19. All negative panel members tested negative throughout the study. Analysis of standard deviation and percent coefficient of variation of the Ct values from valid tests performed on positive panel members (see Table 20 and Table 21) yielded overall CV (%) ranges from 1.5% to 2.6% for TV and from 1.2% to 4.9% for MG.

Table 19 Summary of within laboratory precision

Target Concentration		N Tested	N positive TV	N positive MG	Hit Rate		95% Confidence Interval			
							TV		MG	
TV	MG				TV	MG	Lower Limit	Upper Limit	Lower Limit	Upper Limit
Vaginal Swab collected in **cobas**® PCR Media										
Neg	Neg	72	0	0	0.0%	0.0%	0.0%	5.0%	0.0%	5.0%
0.06 cells/mL	1.2 cp/mL	72	48	61	66.7%	84.7%	54.6%	77.3%	74.3%	92.1%
0.24 cells/mL	4.8 cp/mL	71	69	70	97.2%	98.6%	90.2%	99.7%	92.4%	100.0%
0.73 cells/mL	14.4 cp/mL	72	72	72	100.0%	100.0%	95.0%	100.0%	95.0%	100.0%
Urine stabilized in **cobas**® PCR Media										
Neg	Neg	72	0	0	0.0%	0.0%	0.0%	5.0%	0.0%	5.0%

Target Concentration		N Tested	N positive TV	N positive MG	Hit Rate		95% Confidence Interval			
							TV		MG	
TV	MG				TV	MG	Lower Limit	Upper Limit	Lower Limit	Upper Limit
0.02 cells/mL	0.2 cp/mL	72	44	53	61.1%	73.6%	48.9%	72.4%	61.9%	83.3%
0.07 cells/mL	0.8 cp/mL	72	72	72	100.0%	100.0%	95.0%	100.0%	95.0%	100.0%
0.20 cells/mL	2.5 cp/mL	72	72	72	100.0%	100.0%	95.0%	100.0%	95.0%	100.0%
Meatal Swab collected in **cobas**® PCR Media										
Neg	Neg	72	N/A	0	N/A	0.0%	N/A	N/A	0.0%	5.0%
0.01 cells/mL	0.1 cp/mL	72	N/A	41	N/A	56.9%	N/A	N/A	44.7%	68.6%
0.05 cells/mL	0.5 cp/mL	72	N/A	69	N/A	95.8%	N/A	N/A	88.3%	99.1%
0.16 cells/mL	1.6 cp/mL	72	N/A	72	N/A	100.0%	N/A	N/A	95.0%	100.0%
Cervical specimens collected in PreservCyt® Solution										
Neg	Neg	72	0	N/A	0.0%	N/A	0.0%	5.0%	N/A	N/A
0.03 cells/mL	0.3 cp/mL	72	39	N/A	54.2%	N/A	42.0%	66.0%	N/A	N/A
0.11 cells/mL	1.1 cp/mL	72	69	N/A	95.8%	N/A	88.3%	99.1%	N/A	N/A
0.33 cells/mL	3.3 cp/mL	72	72	N/A	100.0%	N/A	95.0%	100.0%	N/A	N/A

Table 20 Overall mean, standard deviations and coefficients of variation (%) for cycle threshold, TV positive panels

Target Concentration	Hit Rate	Mean Ct	Within run		Between run		Between day		Between instrument		Between lot		Total	
TV			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Vaginal Swab collected in **cobas**® PCR Media														
0.06 cells/mL	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
0.24 cells/mL	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
0.73 cells/mL	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														
0.02 cells/mL	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
0.07 cells/mL	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
0.20 cells/mL	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														
0.03 cells/mL	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
0.11 cells/mL	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
0.33 cells/mL	100.0%	34.6	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 21 Overall mean, standard deviations and coefficients of variation (%) for cycle threshold, MG positive panels

Target Concentration	Hit Rate	Mean Ct	Within run		Between run		Between day		Between instrument		Between lot		Total	
MG			**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV %**
Vaginal Swab collected in **cobas**® PCR Media														
1.2 cp/mL	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
4.8 cp/mL	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
14.4 cp/mL	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														
0.2 cp/mL	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
0.8 cp/mL	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
2.5 cp/mL	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														
0.1 cp/mL	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
0.5 cp/mL	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
1.6 cp/mL	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

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 22 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 3 x LoD). None of the organisms tested interfered with the test performance by generating false positive results. Detection of TV and MG target was not affected by organisms tested except *Trichomonas tenax* at concentration levels > 1E+04 CFU/mL. *Trichomonas tenax* is a commensal of the oral cavity.

Table 22 Microorganisms tested for analytical specificity/cross reactivity

Microorganism	Concentration	Microorganism	Concentration
Acholeplasma laidlawii	1.0E+06 CFU/mL	*Klebsiella oxytoca*	1.0E+06 CFU/mL
Acholeplasma oculi	1.0E+06 CFU/mL	*Klebsiella pneumoniae*	1.0E+06 CFU/mL
Achromobacter xerosis	1.0E+06 CFU/mL	*Lactobacillus acidophilus*	1.0E+06 CFU/mL
Acinetobacter lwoffi	1.0E+06 CFU/mL	*Lactobacillus crispatus*	1.0E+06 CFU/mL
Actinomyces israelii	1.0E+06 CFU/mL	*Lactobacillus jensenii*	1.0E+06 CFU/mL
Aerococcus viridans	1.0E+06 CFU/mL	*Lactobacillus vaginalis*	1.0E+06 CFU/mL
Aeromonas hydrophila	1.0E+06 CFU/mL	*Leptotrichia buccalis*	1.0E+06 CFU/mL
Alcaligenes faecalis subsp. faecalis	1.0E+06 CFU/mL	*Leuconostoc mesenteroides subsp. mesenteroides*	1.0E+06 CFU/mL
Atopobium vaginae	1.0E+06 CFU/mL	*Leuconostoc paramesenteroides*	1.0E+06 CFU/mL
Bacillus subtilis	1.0E+06 CFU/mL	*Listeria monocytogenes*	1.0E+06 CFU/mL
Bacteroides fragilis	1.0E+06 CFU/mL	*Micrococcus luteus*	1.0E+06 CFU/mL
Bacteroides ureolyticus	1.0E+06 CFU/mL	*Mobiluncus curtisii subsp. curtisii*	1.0E+06 CFU/mL

Bifidobacterium adolescentis	1.0E+06 CFU/mL	*Moraxella osloensis*	1.0E+06 CFU/mL
Branhamella catarrhalis	1.0E+06 CFU/mL	*Moraxella catarrhalis*	1.0E+06 CFU/mL
Brevibacterium linens	1.0E+06 CFU/mL	*Moraxella lacunata*	1.0E+06 CFU/mL
Campylobacter jejuni	1.0E+06 CFU/mL	*Morganella morganii*	1.0E+06 CFU/mL
Candida albicans	1.0E+06 CFU/mL	*Mycobacterium smegmatis*	1.0E+06 CFU/mL
Candida glabrata	1.0E+06 CFU/mL	*Mycoplasma faucium*	1.0E+06 CFU/mL
Candida parapsilosis	1.0E+06 CFU/mL	*Mycoplasma fermentans*	1.0E+06 CFU/mL
Candida tropicalis	1.0E+06 CFU/mL	*Mycoplasma hominis*	1.0E+06 CFU/mL
Chlamydia trachomatis	1.0E+06 CFU/mL	*Mycoplasma orale*	1.0E+06 CFU/mL
Chromobacterium violaceum	1.0E+06 CFU/mL	*Mycoplasma penetrans*	1.0E+06 CFU/mL
Citrobacter braakii	1.0E+06 CFU/mL	*Mycoplasma pirum*	1.0E+06 CFU/mL
Clostrodium perfringens	1.0E+06 CFU/mL	*Mycoplasma pneumoniae*	1.0E+06 CFU/mL
Clostrodioides difficile serogroup B	1.0E+06 CFU/mL	*Mycoplasma primatum*	1.0E+06 CFU/mL
Corynebacterium genitalium	1.0E+06 CFU/mL	*Mycoplasma salivarium DNA*	1.0E+06 cp/mL
Corynebacterium xerosis	1.0E+06 CFU/mL	*Mycoplasma spermatophilum*	1.0E+06 ccu/mL
Cryptococcus neoformans	1.0E+06 CFU/mL	*Neisseria gonorrhoeae*	1.0E+06 CFU/mL
Cytomegalovirus	1.0E+05 IU/mL	*Pentatrichomonas hominis*	1.0E+06 CFU/mL
Derxia gummosa	1.0E+06 CFU/mL	*Peptostreptococcus anaerobius*	1.0E+06 CFU/mL
Dientamoeba fragilis	1.0E+06 CFU/mL	*Prevotella bivia*	1.0E+06 CFU/mL
Eikenella corrodens	1.0E+06 CFU/mL	*Propionibacterium acnes*	1.0E+06 CFU/mL
Enterobacter aerogenes	1.0E+06 CFU/mL	*Proteus mirabilis*	1.0E+06 CFU/mL
Enterobacter cloacae	1.0E+06 CFU/mL	*Providencia stuartii*	1.0E+06 CFU/mL
Enterococcus avium	1.0E+06 CFU/mL	*Pseudomonas aeruginosa*	1.0E+06 CFU/mL
Enterococcus faecalis	1.0E+06 CFU/mL	*Rahnella aquatilis*	1.0E+06 CFU/mL
Enterococcus faecium	1.0E+06 CFU/mL	*Rhizobium radiobacter*	1.0E+06 CFU/mL
Erysipelothrix rhusiopathiae	1.0E+06 CFU/mL	*Rhodospirillum rubrum*	1.0E+06 CFU/mL
Escherichia coli	1.0E+06 CFU/mL	*Saccharomyces cerevisiae*	1.0E+06 CFU/mL
Flavobacterium meningosepticum	1.0E+06 CFU/mL	*Salmonella minnesota*	1.0E+06 CFU/mL
Fusobacterium nucleatum	1.0E+06 CFU/mL	*Serratia marcescens*	1.0E+06 CFU/mL
Gardnerella vaginalis	1.0E+06 CFU/mL	*Staphylococcus aureus MSSA NRS 164*	1.0E+06 CFU/mL
Gemella haemolysans	1.0E+06 CFU/mL	*Staphylococcus epidermidis*	1.0E+06 CFU/mL
Giardia intestinalis	1.0E+06 CFU/mL	*Streptococcus agalactiae*	1.0E+06 CFU/mL
Haemophilus ducreyi	1.0E+06 CFU/mL	*Streptococcus pneumoniae*	1.0E+06 CFU/mL
Herpes Simplex Virus Type 1	1.0E+05 cp/mL	*Streptococcus pyogenes*	1.0E+06 CFU/mL
Herpes Simplex Virus Type 2	1.0E+05 cp/mL	*Trichomonas tenax*	1.0E+04 CFU/mL*
Mycoplasma hominis	1.0E+06 CFU/mL	*Ureaplasma urealyticum*	1.0E+06 ccu/mL
Human immunodeficiency virus	1.0E+05 cp/mL	*Veillonella parvula*	1.0E+06 CFU/mL
Human Papillomavirus type 16	1.0E+05 cells/mL	*Vibrio parahaemolyticus*	1.0E+06 CFU/mL
Kingella denitrificans	1.0E+06 CFU/mL	*Yersinia enterocolitica*	1.0E+06 CFU/mL

*Level at which no interference with TV detection observed, tested also at 1.0E+06 CFU/mL which showed interference with TV, but not with MG

Interference

The effect of over-the-counter or prescription feminine products that may be present in urogenital specimens (Table 23) were evaluated. Testing was done using pooled clinical and contrived specimens spiked with potential interferents at levels expected from normal patient usage and in absence and presence of TV and MG target (spiked at approximately 3 x LoD).

Of the over-the-counter (OTC) feminine hygiene and prescription products tested in urogenital specimens, Metronidazole Vaginal Gel by Sandoz, Replens™ and RepHresh™ produced false negative or invalid results. These products contain carbomer(s). Products containing carbomer(s) have been shown to generate false negative and invalid results. Table 23 is not intended to be a comprehensive list of carbomer containing products.

Table 23 List of substances tested for interference in urogenital specimens

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

* Metronidazole Vaginal Gel by Sandoz, Replens™ and RepHresh™ showed interference at levels that may potentially be present in clinical specimens.
**Products containing metronidazole which did not show interference, in contrast to the Metronidazole Vaginal Gel by Sandoz.

Endogenous substances that may be present in urogenital specimens were tested for interference. Testing was done using pooled clinical and contrived specimens spiked with potential interferents at elevated levels and in absence and presence of TV and MG target (spiked at approximately 3 x LoD).

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 24.

Table 24 Summary of endogenous substance concentrations that do not show interference

Interferent	Endocervical Swab	Meatal Swab	Cervical 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

Competitive inhibition

To assess competitive inhibition between TV and MG, samples of each specimen type (swabs and meatal swabs in **cobas**® PCR Media, urine stabilized in **cobas**® PCR Media and cervical specimens in PreservCyt® Solution) were tested. Low and moderate concentrations of one target were mixed with very high concentrations of the opposite target. Low and moderate concentrations were defined as ~1 x LoD and ~3 x LoD, respectively, and high concentrations were defined as those generating a signal greater than in 95% of target positive clinical specimens.

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

Whole system failure

The samples tested in the whole system failure study were pooled negative urine stabilized in **cobas**® PCR Media, as well as contrived matrices equivalent to vaginal and meatal swab specimens collected in **cobas**® PCR Media or cervical specimens collected in PreservCyt® Solution, co-spiked with TV and MG target to a concentration of approximately 3 x LoD of the respective target and matrix. The results of this study determined that all replicates were valid and positive for TV and MG, resulting in a whole system failure rate of 0%. The two-sided 95% exact confidence interval was 0% for the lower bound and 3.6% for the upper bound [0%: 3.6%].

Cross contamination

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) for TV and 0.0% (0/480) for MG when alternating very high positive and negative samples were tested over multiple runs. 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. The likelihood of encountering such specimens in the routine use of **cobas**® TV/MG is proportional to TV prevalence in the testing population. Therefore the sample to sample cross-contamination rate for TV in routine use of **cobas**® TV/MG will likely be less than 0.7% x 5% x TV prevalence in the testing population. With the prevalence of 8.1%[1] in female patients, the cross-contamination rate would be 0.7% x 5% x 8.1% = 0.003%.

Clinical performance evaluation

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 25 and Table 26.

Table 25 Determination of TV PIS as derived from vaginal swabs for women 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 26 Determination of MG PIS as derived from vaginal swabs for women 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.

Results

A total of 2,194 subjects were enrolled and across all specimen types, 6807 samples were tested on **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.

TV clinical performance

Table 27 and Table 28 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 27 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**

Note: 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 28 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**

Note: Asymp = asymptomatic; Symp = symptomatic.

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 29.

Table 29 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.

Expected values for TV

Positivity rate

Table 30 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] ES = endocervical swab, PC = PreservCyt, UR = urine, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal 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

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 31 through Table 35, respectively, per specimen type.

Table 31 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
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 32 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 33 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 34 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 35 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

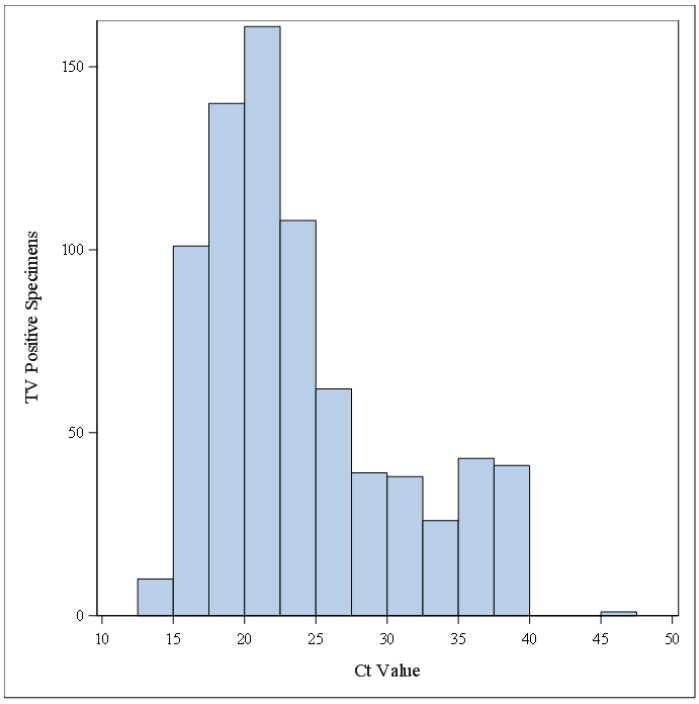
Note: NPV = Negative predictive value; PPV = Positive predictive value.

[a] The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG V/MG to patient infected status.

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 7.

Figure 7 Cycle threshold distribution of TV positive specimens



MG clinical performance

Table 36 and Table 37 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 36 MG positive/negative analysis for female PIS

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

Note: Asymp = asymptomatic, Symp = symptomatic.

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: ES = endocervical swab, UR = urine, VS = vaginal swab, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal swab.

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.

Table 37 MG positive/negative analyses for male PIS

Patient Infected Status	NAAT1 UR	NAAT2 UR	NAAT3 UR	cobas® TV/MG UR	cobas® TV/MG MS-C/ MS-S	Symptom Status Symp	Symptom Status 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**

Note: 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 P IS 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 38.

Table 38 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)	(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)	(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)	(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)	(73.9%, 91.9%)	97.9% (957/978)	(96.7%, 98.6%)	5.8	70.8	99.1

[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.

Expected values for MG

Positivity rate for MG

Table 39 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%)
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%)

[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.

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 40 through Table 45, respectively, per specimen type.

Table 40 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 41 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

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 42 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 43 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 44 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

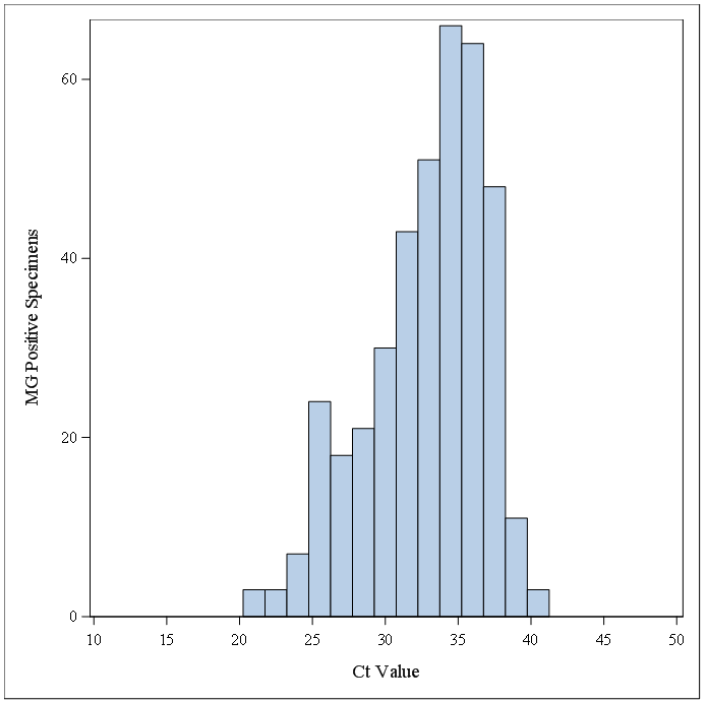
Note: NPV = Negative predictive value; PPV = Positive predictive value.

[a] The sensitivity and specificity were estimated by comparing the test results with **cobas**® TV/MG to patient infected status.

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 8.

Figure 8 Cycle threshold distribution of MG positive specimens



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, PreservCyt®, 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 45 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, NPA = negative percent agreement, PPA = positive percent agreement.

System equivalency

System equivalency of the **cobas**® 5800, **cobas**® 6800 and **cobas**® 8800 Systems was demonstrated via performance studies. The data presented in this Instructions for Use support equivalent performance for all systems.

Additional information

Key assay features

Sample types

- Endocervical swab collected in **cobas**® PCR Media
- Vaginal swab collected in **cobas**® PCR Media
- Self-collected Vaginal swab collected in **cobas**® PCR Media
- Meatal swab collected in **cobas**® PCR Media
- Self-collected Meatal swab collected in **cobas**® PCR Media
- Male and female urine stabilized in **cobas**® PCR Media
- Cervical specimens collected in PreservCyt® Solution

Amount of sample required/processed

- ≥1000 µL required in sample tube for swab samples, instrument processes 400 µL
- ≥ 1000 µL required in sample tube for PreservCyt® samples, instrument processes 400 µL
- ≥ 1200 µL required in sample tube for meatal swab samples, instrument processes 850 µL
- ≥ 1200 µL required in sample tube for urine samples, instrument processes 850 µL
- On **cobas**® 5800 System, ≥3000 µL required in sample tube for PreservCyt® samples in primary tubes, instrument processes 400 µL

Test duration

- < 3.5 hours to first result

Symbols

The following symbols are used in labeling for Roche PCR diagnostic products.

Table 46 Symbols used in labeling for Roche PCR diagnostics products

Age/DOB Age or Date of Birth	Device not for near-patient testing	QS IU/PCR QS IU per PCR reaction, use the QS International Units (IU) per PCR reaction in calculation of the results.
SW Ancillary Software	Device not for self-testing	
Assigned Range [copies/mL] Assigned Range (copies/mL)	Distributor *(Note: The applicable country/region may be designated beneath the symbol)*	SN Serial number
Assigned Range [IU/mL] Assigned Range (IU/mL)	Do not re-use	Site Site
EC REP Authorized representative in the European Community	Female	Procedure Standard Standard Procedure
BARCODE Barcode Data Sheet	For IVD performance evaluation only	STERILE EO Sterilized using ethylene oxide
LOT Batch code	GTIN Global Trade Item Number	Store in dark
Biological risks	Importer	Temperature limit
REF Catalogue number	IVD In vitro diagnostic medical device	TDF Test Definition File
CE CE marking of conformity; this device is in conformity with the applicable requirements for CE marking of an in vitro diagnostic medical device	LLR Lower Limit of Assigned Range	This way up
	Male	Procedure UltraSensitive Ultrasensitive Procedure
Collect Date Collect date	Manufacturer	UDI Unique Device Identifier
Consult instructions for use	CONTROL − Negative control	ULR Upper Limit of Assigned Range
Σ Contains sufficient for <*n*> tests	NON STERILE Non-sterile	Urine Fill Line Urine Fill Line
CONTENT Content of kit	Patient Name	Rx Only US Only: Federal law restricts this device to sale by or on the order of a physician.
CONTROL Control	Patient number	Use-by date
Date of manufacture	Peel here	
Device for near-patient testing	CONTROL + Positive control	
Device for self-testing	QS copies / PCR QS copies per PCR reaction, use the QS copies per PCR reaction in calculation of the results.	

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Technical support

For technical support (assistance) please reach out to your local affiliate:
https://www.roche.com/about/business/roche_worldwide.htm

Manufacturer

Table 47 Manufacturer

Manufactured in the United States

Roche Molecular Systems, Inc.
1080 US Highway 202 South
Branchburg, NJ 08876 USA
www.roche.com

Made in USA

Trademarks and patents

See https://diagnostics.roche.com/us/en/about-us/patents

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Document revision

Document Revision Information	
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