March 21, 2018

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

Re: K173887
Trade/Device Name: cobas CT/NG for use on cobas 6800/8800 systems
Regulation Number: 21 CFR 866.3390
Regulation Name: Neisseria spp. direct serological test reagents
Regulatory Class: Class II
Product Code: LSL, MKZ, OOI
Dated: December 20, 2017
Received: December 21, 2017

Dear Nobuko Nakajima:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR

Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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

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

Sincerely,

Tamara V. Feldblyum -S for

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

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K173887

Device Name
cobas® CT/NG for use on the cobas® 6800/8800 Systems

Indications for Use *(Describe)*
The cobas® CT/NG on the cobas® 6800/8800 system is an automated, qualitative in vitro nucleic acid diagnostic test, that utilizes real-time polymerase chain reaction (PCR), for the direct detection of Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG) DNA in male and female urine, clinician-instructed self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical swab specimens, all collected in cobas® PCR Media (Roche Molecular Systems, Inc.), and cervical specimens collected in PreservCyt® solution. This test is intended as an aid in the diagnosis of chlamydial and gonococcal disease in both symptomatic and asymptomatic individuals.

Ancillary Collection Kits:
The cobas® PCR Media Dual Swab Sample Kit is used to collect and transport endocervical and vaginal swab specimens. The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for gynecological specimens.
Note: This kit has been validated for use with the following tests:
• cobas® CT/NG v2.0 Test
• cobas® CT/NG for use on cobas® 6800/8800 Systems

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

The cobas® PCR Urine Sample Kit is used to collect and transport urine specimens. The cobas® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens. Use this collection kit only with either cobas® CT/NG on cobas® 6800/8800 Systems or the cobas® CT/NG v2.0 Test.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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cobas® CT/NG
for use on the **cobas**® 6800/8800 Systems
510(k) Summary

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

Submitter Name	Roche Molecular Systems, Inc.
Address	4300 Hacienda Drive Pleasanton, CA, 94588-2722
Contact	Nobuko Nakajima Phone: (925)730-8215 FAX: (925)225-0207 Email: nobuko.nakajima@roche.com
Date Prepared	December 4, 2017
Proprietary Name	**cobas**® CT/NG for use on **cobas**® 6800/8800 systems
Common Name	Real-time PCR assay, in vitro nucleic acid amplification test for the quantitative detection of Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG)
Classification Name	Sec. 866.3390 Neisseria spp. direct serological test reagents Sec. 866.3120 Chlamydia serological reagents, Sec. 862.2570 Real Time Nucleic Acid Amplification System
Product Codes	LSL MKZ OOI
Predicate Devices	**cobas**® CT/NG v2.0 Test (K163184)
Establishment Registration	Roche Molecular Systems, Inc. (2243471)

1. DEVICE DESCRIPTION

cobas® CT/NG is a new qualitative test performed on the **cobas**® 6800 System and **cobas**® 8800 System. **cobas**® CT/NG enables the detection of CT/NG DNA in endocervical, vaginal, urine and cervical specimens of infected female patients and urine specimens in infected male patients. Target-specific primers and two probes are used to detect but not discriminate between the CT cryptic plasmid and the ompA gene. Additionally, target-specific primers and two probes are used to detect but not discriminate between two conserved sequences in the NG DR-9 region. 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.

1.1. Principles of the procedure

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

Nucleic acid from patient samples, 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 which are selected from highly conserved plasmid and genomic regions of CT and NG. A region on the CT cryptic plasmid and the ompA gene (dual target) and two conserved sequences of the NG DR-9 region are amplified by **cobas**® CT/NG.

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 CT or NG 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. However, newly formed amplicons are not eliminated since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

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

Figure 1: cobas® CT/NG on the cobas® 6800/8800 system

2. INTENDED USE

The **cobas**® CT/NG on the **cobas**® 6800/8800 system is an automated, qualitative in vitro nucleic acid diagnostic test, that utilizes real-time polymerase chain reaction (PCR), for the direct detection of *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) DNA in male and female urine, clinician-instructed self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical swab specimens, all collected in **cobas**® PCR Media (Roche Molecular Systems, Inc.), and cervical specimens collected in PreservCyt® solution. This test is intended as an aid in the diagnosis of chlamydial and gonococcal disease in both symptomatic and asymptomatic individuals.

2.1. Ancillary Collection Kits

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

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

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

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

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

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

The **cobas**® PCR Urine Sample Kit is used to collect and transport urine specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens. Use this collection kit only with either **cobas**® CT/NG on **cobas**® 6800/8800 Systems or the **cobas**® CT/NG v2.0 Test.

3. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the RMS **cobas**® CT/NG for use on the **cobas**® 6800/8800 systems are substantially equivalent to other legally marketed nucleic acid amplification tests intended for the qualitative detection of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG).

As indicated in Table 1, the **cobas**® CT/NG for use on the **cobas**® 6800/8800 systems is substantially equivalent to significant characteristics of the identified predicate device, the currently cleared **cobas**® CT/NG v2.0 Test (K163184).

Table 1: Comparison of the cobas® CT/NG for use on the cobas® 6800/8800 systems with the Predicate Device

	Predicate Device: cobas® CT/NG v2.0 Test (K163184)	**Submitted Device cobas® CT/NG for use on the cobas® 6800/8800 systems**
Intended Use	The **cobas**® CT/NG v2.0 Test is an automated, in vitro nucleic acid amplification test for the qualitative detection of *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) DNA in urogenital specimens. The Test utilizes the Polymerase Chain Reaction (PCR) for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in male and female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical swab specimens, all collected in **cobas**® PCR Media (Roche Molecular Systems, Inc.), and cervical specimens collected in PreservCyt® solution. This test is intended as an aid in the diagnosis of chlamydial and gonococcal disease in both symptomatic and asymptomatic individuals.	The **cobas**® CT/NG on the **cobas**® 6800/8800 system is an automated, qualitative in vitro nucleic acid diagnostic test, that utilizes real-time polymerase chain reaction (PCR), for the direct detection of *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) DNA in male and female urine, clinician instructed self-collected vaginal swab specimens (collected in a clinical setting), clinician-collected vaginal swab specimens, and endocervical swab specimens, all collected in **cobas**® PCR Media (Roche Molecular Systems, Inc.), and cervical specimens collected in PreservCyt® solution. This test is intended as an aid in the diagnosis of chlamydial and gonococcal disease in both symptomatic and asymptomatic individuals.

	Predicate Device: **cobas® CT/NG v2.0 Test** **(K163184)**	**Submitted Device** **cobas® CT/NG for use on the** **cobas® 6800/8800 systems**
Intended Use,cont.	**Ancillary Collection Kits:** The **cobas**® PCR Media Dual Swab Sample Kit is used to collect and transport endocervical and vaginal swab specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for gynecological specimens. Use this collection kit only with the **cobas**® CT/NG v2.0 Test. The **cobas**® PCR Media Uni Swab Sample Kit is used to collect and transport human specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for human specimens. Use this collection kit with **cobas**® CT/NG v2.0 Test and **cobas**® Cdiff Tests. The **cobas**® PCR Urine Sample Kit is used to collect and transport urine specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens. Use this collection kit only with the **cobas**® CT/NG v2.0 Test.	**Ancillary Collection Kits:** The **cobas**® PCR Media Dual Swab Sample Kit is used to collect and transport endocervical and vaginal swab specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for gynecological specimens. Note: This kit has been validated for use with the following tests: **cobas**® CT/NG v2.0 Test **cobas**® CT/NG for use on **cobas**® 6800/8800 Systems. The **cobas**® PCR Media Uni Swab Sample Kit is used to collect and transport human specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for human specimens Note: This kit has been validated for use with the following tests: **cobas**® CT/NG v2.0 Test **cobas**® CT/NG for use on **cobas**® 6800/8800 Systems **cobas**® Cdiff Test for use on the **cobas**® 4800 System The **cobas**® PCR Urine Sample Kit is used to collect and transport urine specimens. The **cobas**® PCR Media serves as a nucleic acid stabilizing transport and storage medium for urine specimens Use this collection kit only with either **cobas**® CT/NG on **cobas**® 6800/8800 Systems or the **cobas**® CT/NG v2.0 Test.
Sample Types	• Male and female urine, • Self-collected/clinician-collected vaginal swab specimens in **cobas**® PCR Media, • Endocervical swab specimens in **cobas**® PCR Media, • Cervical specimens in PreservCyt® solution	Same
Subject Status	Asymptomatic and symptomatic	Same
Sample Collection Devices	**cobas**® PCR Media Dual Swab Sample Kit **cobas**® PCR Media Uni Swab Sample Kit **cobas**® PCR Urine Sample Kit	Same
CT Analyte targets	CT cryptic plasmid DNA CT ompA gene	Same
NG Analyte targets	NG genomic DNA	Same

	Predicate Device: **cobas® CT/NG v2.0 Test** **(K163184)**	Submitted Device **cobas® CT/NG for use on the cobas® 6800/8800 systems**
Sample Preparation Procedure	Semi-automated	Automated
Amplification Technology	Real-time PCR	Same
Detection Chemistry	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)	Same
Result Analysis	Based on PCR cycle threshold analysis	Same
Analyzer	**cobas®** 4800 System	**cobas®** 6800/8800 systems

4. NON-CLINICAL PERFORMANCE EVALUATION

4.1. Limit of Detection (LoD)

Analytical sensitivity (Limit of Detection or LoD) was determined by analyzing a dilution series of quantified cultures of *Chlamydia trachomatis* (serovars D and I) and *Neisseria gonorrhoeae* isolates 2948 (ATCC 19424) and 891. CT and NG cultures were diluted into a matrix of pooled negative specimens of each sample type and 70-78 replicates were tested for each level in each specimen type. All levels were analyzed across 3 unique lots of reagents. LoD for each specimen type is shown in Table 2 as the target concentration which can be detected in ≥ 95% of the replicates for all lots.

Table 2: Analytical sensitivity (Limit of Detection)

Specimen Types	***C. trachomatis***				***N. gonorrhoeae***			
	Serovar D		**Serovar I**		**Strain 2948**		**Strain 891**	
	LOD (IFU/mL)	**Mean Ct Value**	**LOD (IFU/mL)**	**Mean Ct Value**	**LOD (CFU/mL)**	**Mean Ct Value**	**LOD (CFU/mL)**	**Mean Ct Value**
Endocervical Swab in **cobas®** PCR	0.3	36.6	1.4	37.1	0.4	36.3	0.08	37.5
Vaginal Swab in	0.3	37.3	1.4	37.0	0.4	36.3	0.08	37.0
cobas® PCR	0.2	37.8	1.3	37.1	0.2	36.3	0.04	38.3

Cervical Samples collected into PreservCyt® Solution	0.6	37.4	2.9	37.4	0.2	36.7	0.08	37.5

IFU = Inclusion Forming Unit; quantification of the same *C. trachomatis* culture using DFA method equates 1 IFU to 6.6 signal generating units (SGU) for Serovar D, and 13.9 SGU for serovar I, where SGU includes Elementary Bodies as well as Reticulate Bodies of *C. trachomatis*

CFU = Colony Forming Units

4.2. Inclusivity

Inclusivity testing was performed for 13 additional CT serovars, the Swedish new variant strain (nvCT) and an additional 43 independently isolated strains of NG using one lot of reagents. Testing was performed using CT and NG cultures diluted into pools of negative specimens. Results are shown in Table 3 and Table 4 for CT serovars and NG strains, respectively. Twenty replicates per dilution level were tested for each strain in each specimen type.

Table 3: Inclusivity Testing for CT Serovars

Serovar Type or Variant	Swab* Specimens		Urine Specimens		PreservCyt Specimens	
	IFU/mL	% Pos	IFU/mL	% Pos	IFU/mL	% Pos
A	1.4	100	0.7	100	1.4	100
B	5.9	100	2.9	100	5.9	100
Ba	18.3	100	9.1	100	18.3	100
C	0.6	100	0.3	100	0.6	100
E	6.4	100	3.2	100	6.4	100
F	3.2	100	1.6	100	3.2	100
G	2.9	100	1.5	100	2.9	100
H	9.7	100	4.8	100	9.7	100
J	1.4	100	0.7	100	1.4	100
K	2.0	100	1.0	100	2.0	100
LGV Type 1	5.9	100	3.0	100	5.9	100
LGV Type 2	12.8	100	6.4	100	12.8	100
LGV Type 3	0.7	100	0.4	100	0.7	100
nvCT	0.7	100	0.3	100	0.7	100

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

Table 4: Inclusivity Testing for NG strains

Numbers of NG Strains	Swab* Specimens	
	CFU/mL	% Pos
39	0.4	≥ 95
4	1.0	≥ 95
Total = 43		
Numbers of NG Strains	**Urine Specimens**	
	CFU/mL	**% Pos**
41	0.2	≥ 95
2	0.5	100
Total = 43		
Numbers of NG Strains	**PreservCyt Specimens**	
	CFU/mL	**% Pos**
42	0.4	≥ 95
1	1.0	100
Total = 43		

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

4.3. Precision

In-house precision was examined using a panel composed of CT and NG cultures diluted into a pool of negative endocervical swab specimen matrix collected in **cobas**® PCR Media, a pool of negative urine matrix plus **cobas**® PCR Media and a pool of negative cervical specimen matrix collected in PreservCyt® Solution. Endocervical swabs were intended to represent all swab samples collected in **cobas**® PCR Media (endocervical and vaginal). Four levels were tested using CT serovar D and NG strain 2948 (ATCC 19424) as the target organisms.

The precision panel was designed to include members with high negative, low and moderate concentrations of CT and NG for each panel matrix, corresponding to ~0.3x, ~1x and ~3x LoD. Testing was performed with three lots of cobas® CT/NG reagents and two instruments for a total of 24 runs. A description of the precision panels and the study performance hit rate is shown in Table 5. 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 6 and Table 7) yielded overall CV (%) ranges from 1.62% to 4.05% for CT and from 1.17% to 3.55% for NG. Testing occurred over 12 days, using 2 instruments, with 2 runs per day. Each run consisted of 3 replicates of each sample.

Table 5: Summary of within-laboratory precision

Level	N Tested	N positive CT	N positive NG	Hit Rate		95% CI CT		95% CI NG	
				CT	NG	LL	UL	LL	UL
Endocervical Swab in cobas® PCR Media									
Negative	72	0	0	0%	0%	0.0	5.0	0.0	5.0
High Negative	72	51	32	71%	44%	59	81	33	57
Low	72	69	68	96%	94%	88	99	86	98
Moderate	72	72	72	100%	100%	95	100	95	100
Cervical samples collected into PreservCyt® Solution									
Negative	72	0	0	0%	0%	0.0	5.0	0.0	5.0
High Negative	72	38	47	53%	65%	41	65	53	76
Low	72	72	69	100%	96%	95	100	88	99
Moderate	72	72	72	100%	100%	95	100	95	100
cobas® PCR Media with Urine									
Negative	72	0	0	0%	0%	0.0	5.0	0.0	5.0
High Negative	72	56	56	78%	78%	66	87	66	87
Low	72	71	72	99%	100%	92	100	95	100
Moderate	72	72	72	100%	100%	95	100	95	100

Table 6: Overall mean, standard deviations and coefficients of variation (%) for cycle threshold, CT positive panel members

Level (Hit Rate)	Mean Ct	Between instrument		Between lot		Within run		Between run		Between day		Total	
		SD	CV %	SD	CV %	SD	CV %	SD	CV %	SD	CV %	SD	CV %
Endocervical Swab in cobas® PCR Media													
High Negative (71%)	39.7	0.00	0.00	0.00	0.00	1.27	3.21	0.00	0.00	0.34	0.85	1.32	3.32
Low (96%)	38.5	0.00	0.00	0.04	0.10	1.14	2.96	0.00	0.00	0.48	1.25	1.24	3.22
Moderate (100%)	36.9	0.00	0.00	0.25	0.69	0.54	1.45	0.07	0.18	0.00	0.00	0.60	1.62
Cervical Samples collected into PreservCyt® Solution													
High Negative (53%)	38.3	0.60	1.57	0.52	1.37	1.12	2.92	0.00	0.00	0.00	0.00	1.37	3.58
Low (100%)	36.9	0.21	0.56	0.28	0.76	0.68	1.85	0.00	0.00	0.00	0.00	0.77	2.08
Moderate (100%)	35.6	0.00	0.00	0.20	0.56	0.52	1.46	0.09	0.24	0.02	0.05	0.56	1.59
cobas® PCR Media with Urine													
High Negative (78%)	38.9	0.00	0.00	0.12	0.30	1.25	3.22	0.39	1.01	0.00	0.00	1.32	3.39
Low (99%)	38.3	0.11	0.28	0.00	0.00	1.52	3.97	0.00	0.00	0.29	0.77	1.55	4.05
Moderate (100%)	37.1	0.00	0.00	0.00	0.00	1.05	2.84	0.00	0.00	0.28	0.77	1.09	2.94

Table 7: Overall mean, standard deviations and coefficients of variation (%) for cycle threshold, NG positive panel members

Level (Hit Rate)	Mean Ct	Between instrument		Between lot		Within run		Between run		Between day		Total	
		SD	CV %	SD	CV %	SD	CV %	SD	CV %	SD	CV %	SD	CV %
Endocervical Swab in cobas® PCR Media													
High Negative (44%)	39.1	0.00	0.00	0.31	0.79	0.84	2.14	0.72	1.85	0.57	1.46	1.28	3.28
Low (94%)	38.1	0.00	0.00	0.00	0.00	1.27	3.34	0.00	0.00	0.00	0.00	1.27	3.34
Moderate (100%)	36.5	0.00	0.00	0.24	0.67	0.69	1.89	0.00	0.00	0.15	0.40	0.74	2.04
Cervical Samples collected into PreservCyt® Solution													
High Negative (65%)	39.0	0.34	0.87	0.00	0.00	1.11	2.85	0.08	0.20	0.45	1.16	1.25	3.21
Low (96%)	38.0	0.00	0.00	0.00	0.00	1.25	3.28	0.00	0.00	0.00	0.00	1.25	3.28
Moderate (100%)	35.8	0.00	0.00	0.28	0.78	0.76	2.13	0.00	0.00	0.00	0.00	0.81	2.27
cobas® PCR Media with Urine													
High Negative (78%)	39.1	0.00	0.00	0.26	0.66	1.35	3.46	0.00	0.00	0.18	0.45	1.39	3.55
Low (100%)	36.7	0.14	0.38	0.16	0.42	0.71	1.92	0.00	0.00	0.00	0.00	0.74	2.00
Moderate (100%)	34.9	0.00	0.00	0.16	0.47	0.37	1.06	0.06	0.18	0.00	0.00	0.41	1.17

4.4. Analytical specificity/Cross-reactivity

A panel of 149 bacteria, fungi and viruses, including those commonly found in the male and female urogenital tract, 20 representatives of non-gonorrhoeae Neisseria strains and other phylogenetically unrelated organisms, were tested with **cobas**®CT/NG to assess analytical specificity. The organisms listed in Table 8 were spiked at concentrations of approximately 1 x 10^6 units*/mL for bacteria and approximately 1 x 10^5 units*/mL for viruses into pools of negative vaginal swab specimens in **cobas**® PCR Media, urine stabilized in **cobas**® PCR Media

and cervical specimens in PreservCyt® Solution. Testing was performed with each potential interfering organism alone as well as with each organism mixed with CT and NG cultures at ~3x LoD. Results indicated that none of these organisms interfered with the detection of CT and NG or produced false positive results in the CT/NG negative matrices. (N=3 across the tested specimen types).

*All bacteria were quantified as Colony Forming Units (CFU) except *Chlamydophila pneumonia* and *Chlamydophila psittaci* which were quantified as Elementary Bodies (EB). All viruses were quantified as units/mL as determined by TCID50 Endpoint Dilution Assay. *Trichomonas vaginalis* and HPV16 were quantified as cells/mL.

Table 8: Microorganisms tested for analytical specificity/cross reactivity

Achromobacter xerosis	*Gemella haemolysans*	*Neisseria subflava*
Acinetobacter calcoaceticus	*Haemophilus ducreyi*	*Neisseria weaverii*
Acinetobacter lwoffi	*Haemophilus influenzae*	*Pantoea agglomerans*
Actinomyces israelii	*Helicobacter pylori*	*Paracoccus denitrificans*
Aerococcus viridans	Herpes simplex virus I	*Peptostreptococcus anaerobius*
Aeromonas hydrophila	Herpes simplex virus II**	*Peptostreptococcus asaccharolyticus*
Alcaligenes faecalis	HPV16*	*Peptostreptococcus magnus*
Atopobium vaginae	*Kingella dentrificans*	*Plesiomonas shigelloides*
Bacillus subtilis	*Kingella kingae*	*Propionibacterium acnes*
Bacteriodes fragilis	*Klebsiella oxytoca*	*Proteus mirabilis*
Bacteroides caccae	*Klebsiella pneumoniae*	*Proteus penneri*
Bacteroides ureolyticus	*Lactobacillus acidophillus*	*Proteus vulgaris*
Bergeriella denitrificans	*Lactobacillus brevis*	*Providencia rettgeri*
Bifidobacterium adolescentis	*Lactobacillus crispatus*	*Providencia stuartii*
Bifidobacterium breve	*Lactobacillus jensenii*	*Pseudomonas aeruginosa*
Bifidobacterium longum	*Lactobacillus lactis*	*Pseudomonas fluorescens*
Blautia product	*Lactobacillus leichmannii*	*Pseudomonas putida*
Branhamella catarrhalis	*Lactobacillus oris*	*Rahnella aquatilis*
Brevibacterium linens	*Lactobacillus parabuchnerri*	*Rhizobium radiobacter*
Campylobacter coli	*Lactobacillus reuteri*	*Rhodospirillum rubrum*
Campylobacter jejuni	*Lactobacillus vaginalis*	*Saccharomyces cerevisiae*
Candida albicans	*Lactococcus lactis cremoris*	*Salmonella choleraesuis*
Candida glabrata	*Legionella pneumophila*	*Salmonella minnesota*
Candida parapsilosis	*Leuconostoc paramesenteroides*	*Salmonella typhimurium*
Candida tropicalis	*Listeria monocytogenes*	*Serratia denitrificans*
Chlamydophila pneumoniae	*Micrococcus luteus*	*Serratia marcescens*
Chlamydophila psittaci	*Moraxella lacunata*	*Shigella dysenteriae*
Chromobacter violaceum	*Moraxella osloensis*	*Staphylococcus aureus*
Citrobacter freundii	*Morganella morganii*	*Staphylococcus epidermidis*
Clostridium difficile	*Mycobacterium smegmatis*	*Staphylococcus saprophyticus*
Clostridium perfringens	*Mycoplasma genitalium***	*Streptococcus agalactiae*
Corynebacterium genitalium	*Mycoplasma hominis*	*Streptococcus anginosus*
Corynebacterium xerosis	*Neisseria cinerea*	*Streptococcus bovis*
Cryptococcus neoformans	*Neisseria elongata subsp. elongata*	*Streptococcus dysgalactiae*
Cytomegalovirus**	*Neisseria elongata subsp. nitroreducens*	*Streptococcus equinis*
Deinococcus radiodurans	*Neisseria flava*	*Streptococcus mitis*

Derxia gummosa	*Neisseria flavescens*	*Streptococcus mutans*
Eikenella corrodens	*Neisseria kochi*	*Streptococcus pneumoniae*
Enterobacter aerogenes	*Neisseria lactamica*	*Streptococcus pyogenes*
Enterobacter cloacae	*Neisseria macacae*	*Streptococcus salivarius*
Enterococcus avium	*Neisseria meningitidis Serogroup A*	*Streptococcus sanguis*
Enterococcus casseliflavus	*Neisseria meningitidis Serogroup B*	*Streptomyces griseinus*
Enterococcus faecalis	*Neisseria meningitidis Serogroup C*	*Trichomonas vaginalis*
Enterococcus faecium	*Neisseria meningitidis Serogroup D*	*Trueperella pyogenes*
Erysipelothrix rhusiopathiae	*Neisseria meningitidis Serogroup W135*	*Ureaplasma urealyticum*
Escherichia coli	*Neisseria meningitidis Serogroup Y*	*Veillonela parvula*
Escherichia fergusonii	*Neisseria mucosa*	*Vibrio cholerae*
Flavobacterium meningosepticum	*Neisseria perflava*	*Vibrio parahaemolyticus*
Fusobacterium nucleatum	*Neisseria polysaccharea*	*Yersinia enterocolitica*
Gardnerella vaginalis	*Neisseria sicca*	-

* HPV16 was tested as CaSki cells.

** Organism was tested at a concentration of 1 x 10^4 Units/mL.

***Organism was tested at a concentration of 1 x 10^5 CFU/mL.

4.5. Interference

The effects of over-the-counter or prescription products that may be present in urogenital specimens (Table 9), were evaluated. Testing was done using pooled clinical specimens (vaginal swab, urine and PreservCyt® specimens) with spiking of potential interferents at levels expected from normal patient usage. Interferents were tested in CT/NG negative specimen pools as well as in specimen pools with CT/NG at ~3x LoD. CT serovars D and I and NG strains 2948 (ATCC 19424) and 891 were used in this study. Five replicates each of CT/NG negative and CT/NG positive samples were tested with each product in each specimen type, except for RepHresh™ Odor Eliminating Vaginal Gel and RepHresh™ Clean Balance Gel, which were tested with 2 replicates each to verify interference that had been observed with Replens™ Long-Lasting Vaginal Moisturizer, a product with a similar formulation.

Of the over-the-counter (OTC) and prescription products tested, Metronidazole Vaginal Gel, Replens™ Long-Lasting Vaginal Moisturizer, RepHresh™ Odor Eliminating Vaginal Gel and RepHresh™ Clean Balance produced false negative or invalid results in at least one replicate of the samples tested.

Table 9: List of substances with concentrations tested that do not interference with test performance in urogenital specimens

Product Name	Vaginal Swabs	Urine	PreservCyt Solution
	mg/mL	mg/mL	mg/mL
Clindamycin Phosphate Vaginal Cream	7.1	3.4	1.6
Equate tioconazole 1	3.7	1.7	0.8
Equate Vagicaine Anti-Itch Cream	4.1	2.0	0.9
Estrace	3.8	2.0	1.0
K-Y™ Ultra Gel	5.7	2.7	1.2
Metronidazole Vaginal Gel	0.1*	0.1*	0.2*
Monistat 3 Vaginal Antifungal Combination Pack	3.7	1.7	0.7
Monistat® Complete Care Itch Relief Cream	3.7	1.8	0.9
7 Day Vaginal Cream	3.9	1.8	0.8
Norforms Suppositories	3.4	1.7	0.7
Premarin	6.1	3.1	1.4
Replens™ Long-Lasting Vaginal Moisturizer	0.05*	0.05*	0.2*
Summer's Eve Feminine Deodorant Spray	6.4	3.1	2.0
VCF - Vaginal Contraceptive Foam	2.1	1.0	0.4
Yeast Gard Advanced	3.7	1.7	1.0
Azo Standard (urine only)	N/A	0.1	N/A
RepHresh™ Odor Eliminating Vaginal Gel	‡	‡	‡
RepHresh™ Clean Balance Gel	‡	‡	‡

* Concentrations above this level may cause interference in clinical samples

‡ RepHresh™ products were tested using simulated swab specimen. Concentrations of product that did not interfere with test performance were not determined

Endogenous substances that may be present in urogenital specimens were tested for interference. Testing was done using pooled clinical specimens (endocervical swab, urine and PreservCyt® specimens) with spiking of potential endogenous interferents. Interferents were tested in CT/NG negative specimen pools as well as in the presence of CT/NG at ~3x LoD. CT serovars D and I and NG strains 2948 (ATCC 19424) and 891 were used in this study. Five replicates each of CT/NG negative and CT/NG positive samples were tested with each substance in each specimen type.

Interference was noted with whole blood at 10% for urine and PreservCyt® specimens and with cervical mucus at 1% in endocervical specimens when at least one replicate of the samples tested produced false negative or invalid results . Levels of endogenous substances tolerated by the assay for all specimen types are shown in Table 10.

Table 10: Summary of endogenous substance concentrations that do not show interference

Interferent	Endocervical Swab	PreservCyt®	Urine
Albumin (% w/v)	N/A	N/A	5%
Bilirubin (% w/v)	N/A	N/A	0.5%
Mucus (% w/v)	0.5%	1.0%	0.5%
Glucose (% w/v)	N/A	N/A	1.0%
Peripheral Blood Mononuclear Cells (PBMCs as cells/mL)	1.0E+06	1.0E+06	1.0E+06
pH (acidic and alkaline)	N/A	N/A	pH 4 and pH 9
Semen (% w/v)	1.5%	1.5%	N/A
Whole Blood (% v/v)	10%	5%	5%

4.6. Competitive Inhibition

To assess competitive inhibition between CT and NG, samples of vaginal swab, urine and PreservCyt® specimens were tested with low and moderate concentrations of one target mixed with very high concentrations of the opposite target. Low and moderate concentrations were defined as ~1x LoD and ~3x LoD, respectively, and high concentrations ($\geq 10^3$ IFU/mL for CT and $\geq 10^4$ CFU/mL for NG) were defined as generating a signal greater than observed in 95% of target positive clinical specimens. Testing results indicated that when NG was present at a high concentration, CT was detected in all specimen types, at both low (~1x LoD) and moderate (~3x LoD) levels. Results also indicated that when CT was present at a high concentration, NG was detected in all specimen types at moderate (~3x LoD) levels, however, NG was not consistently detected at low levels (Expanded testing indicated detection in 35% (7/20) of the samples at 0.4 CFU/ml and 60% (12/20) of the samples at 0.65 CFU/ml).

4.7. Cross contamination/Carryover

Studies were performed to evaluate potential cross-contamination on the cobas® 6800/8800 Systems using cobas® CT/NG. Cross-contamination can cause false positive results. In this performance study the sample-to-sample cross-contamination rate of cobas® CT/NG has been determined to be 0.5% (2/432), (95% CI: 0.1%-1.7%) when alternating very high positive and negative samples were tested over nine runs. Run-to-run cross-contamination has not been observed (0/282). Testing was done using samples prepared with cobas® PCR Media and with PreservCyt® Solution and with urine stabilized in cobas® PCR Media. High positive samples (≥103 IFU/mL for CT and ≥104 CFU/mL for NG) in the study were prepared to generate a Ct value that was lower than that obtained with 95% or more of the specimens of infected patients in the intended use population. Cross contamination rates in clinical settings depend on the proportion of high positive samples and prevalence of the disease. Routine clinical cross-contamination rates are expected to be lower than what was observed in this study and need to be assessed in user's settings.

5. CLINICAL PERFORMANCE EVALUATION

5.1. Clinical Performance

5.1.1. Study Design

The clinical utility and performance of **cobas**® CT/NG was established in a multi-site, prospective collection study by comparing the results to a Patient Infected Status (PIS) that used a combination of FDA-cleared NAATs for urogenital specimens. Female and male urogenital specimens were collected at 9 geographically diverse sites in the US with testing performed at 4 laboratory testing sites (3 external and 1 internal).

Prospectively enrolled female subjects provided the following urogenital specimens: first-void urine, 3 vaginal swabs, 1 endocervical swab in **cobas**® PCR Media, and 1 cervical sample in PreservCyt® Solution. If the female was in the clinician-collected vaginal swab arm of the study, 2 of the vaginal swabs were placed in the respective manufacturers' collection device and 1 in **cobas**® PCR Media. If the female subject was in the self-collected vaginal swab self-collection arm of the study, then 1 vaginal swab was self-collected first and placed into **cobas**® PCR Media

and then followed by the 2 clinician-collected vaginal swabs and placed in the 2 respective manufacturers' collection devices.

Prospectively enrolled male subjects provided a urine specimen that was aliquoted into the respective manufacturers' collection device and **cobas**® PCR Media.

Subjects were classified as symptomatic if they self-reported symptoms indicative of a CT or NG infection as listed below:

- Dysuria (pain during urination)
- Coital pain, difficulty or bleeding
- Pelvic pain
- Abnormal vaginal discharge
- Pelvic, uterine or ovarian pain
- Urethral discharge
- Testicular pain
- Scrotal pain or swelling

Prospectively enrolled subjects were classified as asymptomatic if they did not report any of the above symptoms.

Specimens were tested for CT and NG using **cobas**® CT/NG and commercially available FDA-cleared NAATs. All tests were run according to the respective manufacturers' Instructions For Use.

The clinical performance of **cobas**® CT/NG was evaluated by comparing the results from collected specimen types to a pre-specified PIS (Patient Infected Status) algorithm as determined by the combined results from 2 commercially available NAATs for females and 3 commercially available NAATs for males. The PIS algorithms for Female and Male subjects are shown in Table 11 and Table 12, respectively.

For NG, archived prospectively collected female urine, cervical specimens in PreservCyt®, and endocervical swabs were obtained from the clinical study for cobas® CT/NG v2 test on the cobas® 4800 System. The PIS of these specimens were already determined from the clinical study for cobas® CT/NG v2 test on the cobas® 4800 System..

Table 11: Determination of female Patient Infected Status (PIS) for urogenital specimens[a]

NAAT1 Urine/Vaginal	NAAT2 Urine/Vaginal	Patient Infected Status (PIS)[b]
+/+	+/+	Infected
+/+	+/- or -/+	Infected
+/- or -/+	+/+	Infected
+/-	-/+	Infected
-/+	+/- or -/+	Infected
+/-	+/-	Infected (Urine) Non-Infected (Vaginal)
+/- or -/+	-/-	Not Infected
+/+	-/-	Not Infected
-/-	+/+	Not Infected
-/-	+/- or -/+	Not Infected
-/-	-/-	Not Infected

[a] One or more positives in each NAAT (NAAT1 and NAAT2) designates the PIS as Infected. Any other combination of results defines the PIS as Not Infected.

[b] In the scenario where one or more of the sample types are invalid, the remaining sample types with valid results from NAAT1 and NAAT2 must have concordant positive or concordant negative results to determine the PIS as Infected or Not Infected, respectively. For all other cases where one or more of the sample types are invalid, the PIS is indeterminate.

Table 12: Determination of male Patient Infected Status (PIS) for urine specimens

NAAT1 Urine	NAAT2 Urine	NAAT3 Urine	Patient Infected Status (PIS)[a]
+	+	+	Infected
+	+	-	Infected
+	-	+	Infected
-	+	+	Infected
-	-	+	Not Infected
-	+	-	Not Infected
+	-	-	Not Infected
-	-	-	Not Infected

[a] If at least 2 out of the 3 test results are concordant positive or negative then the PIS can be considered as Infected or Not Infected, respectively. If one test result is invalid/missing and the other two test results are discordant then the PIS is indeterminate. If 2 or 3 test results are invalid/missing, then the PIS is indeterminate.

Sensitivity (SENS), specificity (SPEC), positive predictive value (PPV), and negative predictive value (NPV) of **cobas**® CT/NG were calculated separately for the detection of CT or NG using the PIS as the composite reference standard and evaluated by gender, sample type, and symptom status. In addition, the predictive values were calculated based on overall sensitivity and specificity (with all data combined for males and females) for a range of hypothetical prevalence values.

5.1.2. Results

A total of 5,197 subjects were prospectively enrolled, of which 5,105 were eligible for inclusion. Of the 5,105 eligible subjects contributing prospective specimens, 5,053 (99.0%) (3,860 females and 1,193 males) were evaluable and were included in the data analyses. A total of 52 subjects (1.0%) were classified as non-evaluable and excluded from all statistical analyses. There were a total of 371 archived prospectively collected female urogenital samples (urine, cervical specimens in PreservCyt, and endocervical swabs) tested in this clinical study from 295 female subjects. Among the 17,169 samples tested in this study, 19 samples exhibited invalid results on the first run (invalid rate of 0.11% (95%CI: 0.07% ; 0.17%)). Upon repeat testing, 3 samples exhibited valid results.

Table 13 and Table 14 summarize the results from symptomatic and asymptomatic, prospectively enrolled subjects designated as infected or non-infected with CT (females and males, respectively) according to the PIS algorithm. A total of 271 females and 118 males were infected with CT. Symptoms were reported in 45.8% (124/271) of infected and 36.7% (1318/3589) of non-infected females. Symptoms were reported in 53.4% (63/118) of infected and 22.5% (242/1074) of non-infected males.

Table 13: CT positive/negative analyses for female Patient Infected Status

	NAAT1		NAAT2		cobas® CT/NG				Symptom Status[a]		
Patient Infected Status	**UR**	**VS**	**UR**	**VS**	**UR**	**VS**	**PC**	**ES**	**Symp**	**Asymp**	**Total**
Infected	+	+	+	+	+	+	+	+	104	108	212
Infected	-	+	+	+	+	+	+	+	2	7	9
Infected	+	+	+	+	+	+	-	+	1	5	6
Infected	+	+	-	+	+	+	+	+	2	4	6
Infected	+	+	+	+	+	+	-	-	1	4	5
Infected	+	+	+	+	+	+	+	-	1	3	4
Infected	-	+	+	+	-	+	+	+	1	3	4
Infected	-	+	-	+	-	+	+	+	2	2	4
Infected	-	+	-	+	+	+	+	+	2	1	3
Infected	+	-	+	+	+	+	-	-	1	1	2
Infected	+	+	+	+	+	+	Failed	+	0	1	1
Infected	+	+	+	+	+	+	+	Failed	1	0	1
Infected	-	+	+	+	+	-	+	+	0	1	1
Infected	-	+	+	+	+	+	+	-	0	1	1
Infected	-	+	+	+	+	+	-	+	1	0	1
Infected	-	+	+	+	+	+	-	-	0	1	1
Infected	-	+	+	+	-	+	-	-	1	0	1
Infected	-	+	-	+	+	+	+	-	0	1	1
Infected	-	+	-	+	-	+	-	+	0	1	1
Infected	+	-	+	+	+	+	+	+	1	0	1
Infected	+	-	+	+	+	-	-	-	0	1	1
Infected	+	-	-	+	-	+	-	-	1	0	1
Infected	+	-	-	+	-	-	-	-	0	1	1
Infected[b]	+	-	+	-	+	+	-	+	1	0	1
Infected[b]	+	-	+	-	+	+	-	-	1	0	1
Infected[b]	+	-	+	-	+	-	-	-	0	1	1
Total									124	147	271
Non-Infected	-	-	-	-	-	-	-	-	1252	2165	3417
Non-Infected	-	-	-	+	-	-	-	-	6	12	18
Non-Infected	-	Invalid	-	-	-	-	-	-	7	5	12
Non-Infected	-	-	-	-	-	Invalid	-	-	6	4	10
Non-Infected	-	-	-	-	-	+	-	-	1	9	10

	NAAT1		NAAT2		cobas® CT/NG				Symptom Status[a]		
Patient Infected Status	**UR**	**VS**	**UR**	**VS**	**UR**	**VS**	**PC**	**ES**	**Symp**	**Asymp**	**Total**
Non-Infected	-	-	+	-	-	-	-	-	2	7	9
Non-Infected	-	-	-	-	-	-	-	+	5	4	9
Non-Infected	-	-	NA	-	-	-	-	-	2	7	9
Non-Infected	-	-	Invalid	-	-	-	-	-	0	9	9
Non-Infected	-	-	-	-	-	-	-	NA	3	5	8
Non-Infected	+	-	-	-	-	-	-	-	3	3	6
Non-Infected	-	-	-	-	+	-	-	-	1	5	6
Non-Infected	-	+	-	-	-	-	-	-	2	2	4
Non-Infected	-	-	-	-	-	-	+	-	1	3	4
Non-Infected	-	-	-	-	-	NA	-	-	1	3	4
Non-Infected	-	NA	-	-	-	-	-	-	0	4	4
Non-Infected	-	-	-	-	-	-	NA	NA	0	3	3
Non-Infected	-	-	-	NA	-	-	-	-	1	2	3
Non-Infected	NA	-	-	-	-	-	-	-	0	3	3
Non-Infected	Invalid	-	-	-	-	-	-	-	2	1	3
Non-Infected	-	+	-	-	-	+	-	-	2	0	2
Non-Infected	-	-	-	+	-	+	+	+	0	2	2
Non-Infected	-	-	-	+	-	+	+	-	2	0	2
Non-Infected	-	-	-	+	-	+	-	+	1	1	2
Non-Infected	-	-	-	+	-	+	-	-	0	2	2
Non-Infected	-	-	-	-	-	+	+	+	2	0	2
Non-Infected	-	-	-	-	-	-	-	Invalid	2	0	2
Non-Infected	-	-	-	Invalid	-	-	-	-	1	1	2
Non-Infected	-	-	+	+	-	+	-	-	0	1	1
Non-Infected	-	-	+	-	+	-	-	-	0	1	1
Non-Infected	-	-	+	-	-	+	-	-	1	0	1
Non-Infected	-	-	-	+	+	+	+	+	0	1	1
Non-Infected	-	-	-	+	-	-	+	+	1	0	1
Non-Infected	-	-	-	+	+	+	-	+	0	1	1
Non-Infected	-	-	-	+	-	-	-	+	0	1	1
Non-Infected	-	-	-	+	+	+	-	-	0	1	1
Non-Infected	-	-	-	-	-	-	NA	-	0	1	1
Non-Infected	-	-	-	-	-	Invalid	Invalid	Invalid	1	0	1
Non-Infected	-	-	-	-	-	-	Invalid	Invalid	1	0	1

	NAAT1		NAAT2		cobas® CT/NG				Symptom Status[a]		
Patient Infected Status	**UR**	**VS**	**UR**	**VS**	**UR**	**VS**	**PC**	**ES**	**Symp**	**Asymp**	**Total**
Non-Infected	-	-	-	-	-	NA	Invalid	-	1	0	1
Non-Infected	-	-	-	-	-	-	Invalid	-	1	0	1
Non-Infected	-	-	-	-	-	+	+	-	1	0	1
Non-Infected	-	-	-	-	-	-	-	Failed	1	0	1
Non-Infected	-	-	-	-	+	-	-	+	1	0	1
Non-Infected	-	-	-	-	-	+	-	+	1	0	1
Non-Infected	-	-	-	-	Failed	-	-	-	1	0	1
Non-Infected	-	-	-	-	-	Failed	-	-	1	0	1
Non-Infected	-	-	-	Invalid	-	+	+	+	0	1	1
Non-Infected	-	-	NA	+	-	+	-	-	0	1	1
Non-Infected	-	Invalid	-	-	-	Invalid	-	-	1	0	1
Total									1318	2271	3589

[a] Symp = symptomatic, Asymp = asymptomatic.

[b] Infected (Urine), Non-Infected (Swabs).

Note: In the scenario where one or more of the sample types are invalid/not available (NA), for female subjects, the remaining sample types with valid results from NAAT1 and NAAT2 must have concordant positive or concordant negative results to determine the PIS as Infected or Not Infected, respectively. For all other cases where one or more of the sample types are invalid/not available (NA), the PIS is indeterminate.

Note: Female subjects with designated infection status (Infected or Non-Infected) and final valid **cobas**® CT/NG test results are considered evaluable and included in this summary table.

Note: + denotes Positive, - denotes Negative, NA denotes Not Available.

Note: UR = urine, VS = vaginal swab, PC = PreservCyt®, ES = endocervical swab.

Note: cobas Invalid are the sum of instrument amplification/detection errors and samples excluded due to protocol deviations

Note: cobas Failed are hardware, software or operator errors causing no result reported

Table 14: CT positive/negative analysis for male Patient Infected Status

	NAAT1	NAAT2	NAAT3	cobas® CT/NG	Symptom Status[a]		
Patient Infected Status	**UR**	**UR**	**UR**	**UR**	**Symp**	**Asymp**	**Total**
Infected	+	+	+	+	60	55	115
Infected	-	+	+	+	1	0	1
Infected	+	Invalid	+	+	1	0	1
Infected	+	-	+	+	1	0	1
Total Infected					63	55	118
Non-Infected	-	-	-	-	238	819	1057
Non-Infected	-	Invalid	-	-	2	2	4
Non-Infected	Invalid	-	-	-	0	3	3
Non-Infected	-	-	Invalid	-	0	3	3
Non-Infected	NA	-	-	-	1	1	2
Non-Infected	-	-	-	+	0	2	2
Non-Infected	-	-	+	-	0	1	1
Non-Infected	-	+	-	+	1	0	1
Non-Infected	+	-	-	-	0	1	1
Total Non-Infected					242	832	1074*

[a] Symp = symptomatic, Asymp = asymptomatic.

*One subject was missing symptom status and is not presented in this table.

Note: If at least 2 out of the 3 test results, for male subjects, are concordant positive or negative then the PIS can be considered as infected or non-infected, respectively. If one test result is invalid/not available (NA) and the other two test results are discordant then the PIS is indeterminate. If 2 or 3 test results are invalid/not available, then the PIS is indeterminate.

Note: Male subjects with designated patient infection status (Infected or Non-Infected) and final valid **cobas**® CT/NG test results are considered evaluable and included in this summary table.

Note: cobas Invalid are the sum of instrument amplification/detection errors and samples excluded due to protocol deviationsNote: + denotes Positive, - denotes Negative, NA denotes Not Available.

Note: UR = urine.

Sensitivity, specificity, and predictive values of **cobas**® CT/NG for CT as defined by PIS are presented by gender, sample type, and symptom status in Table 15.

Table 15: CT clinical performance compared with Patient Infected Status by gender, sample 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	1441	96.0% (119/124)	(90.9%, 98.3%)		99.8% (1315/1317)	(99.4%, 100.0%)	8.6	98.3	99.6
	Asymp	2418	95.2% (140/147)	(90.5%, 97.7%)		99.6% (2262/2271)	(99.2%, 99.8%)	6.1	94.0	99.7
	Overall	3859	95.6% (259/271)c	(92.4%, 97.4%)		99.7% (3577/3588)	(99.5%, 99.8%)	7.0	95.9	99.7
VS-C	Symp	711	100.0% (63/63)	(94.3%, 100.0%)		99.2% (643/648)	(98.2%, 99.7%)	8.9	92.6	100.0
	Asymp	1225	97.6% (83/85)	(91.8%, 99.4%)		99.0% (1129/1140)	(98.3%, 99.5%)	6.9	88.3	99.8
	Overall	1936	98.6% (146/148)	(95.2%, 99.6%)		99.1% (1772/1788)	(98.6%, 99.4%)	7.6	90.1	99.9
VS-S	Symp	720	100.0% (59/59)	(93.9%, 100.0%)		98.8% (653/661)	(97.6%, 99.4%)	8.2	88.1	100.0
	Asymp	1186	98.4% (60/61)	(91.3%, 99.7%)		99.2% (1116/1125)	(98.5%, 99.6%)	5.1	87.0	99.9
	Overall	1906	99.2% (119/120)	(95.4%, 99.9%)		99.0% (1769/1786)	(98.5%, 99.4%)	6.3	87.5	99.9
PC	Symp	1438	95.1% (116/122)	(89.7%, 97.7%)		99.5% (1309/1316)	(98.9%, 99.7%)	8.5	94.3	99.5
	Asymp	2413	90.3% (131/145)	(84.4%, 94.2%)		99.7% (2261/2268)	(99.4%, 99.9%)	6.0	94.9	99.4
	Overall	3851	92.5% (247/267)	(88.7%, 95.1%)		99.6% (3570/3584)	(99.3%, 99.8%)	6.9	94.6	99.4
ES	Symp	1433	95.9% (116/121)	(90.7%, 98.2%)		99.1% (1300/1312)	(98.4%, 99.5%)	8.4	90.6	99.6
	Asymp	2410	91.1% (133/146)	(85.4%, 94.7%)		99.5% (2253/2264)	(99.1%, 99.7%)	6.1	92.4	99.4
	Overall	3843	93.3% (249/267)	(89.6%, 95.7%)		99.4% (3553/3576)	(99.0%, 99.6%)	6.9	91.5	99.5
Male										
UR	Symp	305	100.0% (63/63)	(94.3%, 100.0%)		99.6% (241/242)	(97.7%, 99.9%)	20.7	98.4	100.0
	Asymp	887	100.0% (55/55)	(93.5%, 100.0%)		99.8% (830/832)	(99.1%, 99.9%)	6.2	96.5	100.0
	Overall	1192*	100.0% (118/118)	(96.8%, 100.0%)		99.7% (1071/1074)	(99.2%, 99.9%)	9.9	97.5	100.0

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

[a] UR = urine, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal swab, PC = PreservCyt®, ES = endocervical swab.

[b] Symp = symptomatic, Asymp = asymptomatic.

[c] Five CT PIS infected females had a CT negative urine specimen with NAAT1 and NAAT2 while they had a CT positive vaginal swab with NAAT1 and NAAT2.

* One subject was missing symptom status and is not presented in this table.

Note: In the scenario where one or more of the sample types are invalid/not available, for female subjects, the remaining sample types with valid results from NAAT1 and NAAT2 must have concordant positive or concordant negative results to determine the PIS as Infected or Non-Infected, respectively. For all other cases where one or more of the sample types are invalid/not available, the PIS is indeterminate.

Note: If at least 2 out of the 3 test results, for male subjects, are concordant positive or negative then the PIS can be considered as infected or non-infected, respectively. If one test result is invalid/not available and the other two test results are discordant then the PIS is indeterminate. If 2 or 3 test results are invalid/not available, then the PIS is indeterminate.

Note: Subjects with designated patient infection status (Infected or Non-Infected) and final valid **cobas**® CT/NG test results are considered evaluable and included in this summary table. An evaluable subject may not have all available sample types or valid test results.

Note: CI = confidence interval, PREV = prevalence, SENS = sensitivity, SPEC = specificity, PPV = positive predictive value, NPV = negative predictive value.

Table 16 and Table 17 summarize the results from symptomatic and asymptomatic subjects designated as infected or non-infected with NG (females and males, respectively) according to the PIS algorithm. A total of 57 females and 87 males were infected with NG. Symptoms were reported in 45.6% (26/57) of infected and 37.2% (1416/3803) of non-infected females. Symptoms were reported in 94.3% (82/87) of infected and 20.2% (223/1105) of non-infected males.

Table 16: NG positive/negative analysis for female Patient Infected Status (prospective specimens)

	NAAT1		NAAT2		cobas® CT/NG				Symptom Status[a]		
Patient Infected Status	**UR**	**VS**	**UR**	**VS**	**UR**	**VS**	**PC**	**ES**	**Symp**	**Asymp**	**Total**
Infected	+	+	+	+	+	+	+	+	20	23	43
Infected	-	+	-	+	-	+	+	+	2	3	5
Infected	+	+	-	+	+	+	+	+	0	2	2
Infected	-	+	-	+	+	+	+	+	2	0	2
Infected	+	+	+	+	+	+	+	Failed	1	0	1
Infected	+	+	+	+	+	+	-	-	0	1	1
Infected	+	+	-	+	-	+	-	-	0	1	1
Infected	-	+	NA	+	+	+	+	-	0	1	1
Infected[b]	+	-	+	-	+	-	-	-	1	0	1
Total									26	31	57

	NAAT1		NAAT2		cobas® CT/NG				Symptom Status[a]		
Patient Infected Status	**UR**	**VS**	**UR**	**VS**	**UR**	**VS**	**PC**	**ES**	**Symp**	**Asymp**	**Total**
Non-Infected	-	-	-	-	-	-	-	-	1368	2315	3683
Non-Infected	-	+	-	-	-	-	-	-	4	11	15
Non-Infected	+	-	-	-	-	-	-	-	5	7	12
Non-Infected	-	-	NA	-	-	-	-	-	2	7	9
Non-Infected	-	Invalid	-	-	-	-	-	-	5	4	9
Non-Infected	-	-	-	-	-	Invalid	-	-	5	3	8
Non-Infected	-	-	-	-	-	-	-	NA	3	5	8
Non-Infected	-	-	Invalid	-	-	-	-	-	0	8	8
Non-Infected	-	-	-	-	-	+	-	-	2	4	6
Non-Infected	-	-	-	-	-	NA	-	-	1	3	4
Non-Infected	-	NA	-	-	-	-	-	-	0	4	4
Non-Infected	-	-	-	-	-	-	NA	NA	0	3	3
Non-Infected	-	-	-	NA	-	-	-	-	1	2	3
Non-Infected	NA	-	-	-	-	-	-	-	0	3	3
Non-Infected	Invalid	-	-	-	-	-	-	-	2	1	3
Non-Infected	+	+	-	-	-	+	-	-	0	2	2
Non-Infected	-	-	-	-	+	-	-	-	2	0	2
Non-Infected	-	-	-	-	-	-	-	Invalid	2	0	2

	NAAT1		NAAT2		cobas® CT/NG				Symptom Status[a]		
Patient Infected Status	**UR**	**VS**	**UR**	**VS**	**UR**	**VS**	**PC**	**ES**	**Symp**	**Asymp**	**Total**
Non-Infected	+	+	-	-	-	-	-	-	0	1	1
Non-Infected	+	+	-	-	-	Invalid	-	-	1	0	1
Non-Infected	-	+	-	-	-	+	+	-	1	0	1
Non-Infected	-	+	-	-	-	+	-	-	1	0	1
Non-Infected	-	-	+	+	+	-	-	-	1	0	1
Non-Infected	-	-	-	+	-	+	-	-	0	1	1
Non-Infected	-	-	-	-	-	-	+	+	0	1	1
Non-Infected	-	-	-	-	-	-	-	+	1	0	1
Non-Infected	-	-	-	-	-	Failed	-	-	1	0	1
Non-Infected	-	-	-	-	Failed	-	-	-	1	0	1
Non-Infected	-	-	-	-	-	-	-	Failed	1	0	1
Non-Infected	-	-	-	-	-	-	NA	-	0	1	1
Non-Infected	-	-	-	-	-	-	Invalid	-	1	0	1
Non-Infected	-	-	-	-	-	NA	Invalid	-	1	0	1
Non-Infected	-	-	-	-	-	-	Invalid	Invalid	1	0	1
Non-Infected	-	-	-	-	-	Invalid	Invalid	Invalid	1	0	1
Non-Infected	-	-	-	-	-	-	Failed	-	0	1	1
Non-Infected	-	-	-	Invalid	-	-	-	-	1	0	1
Non-Infected	-	Invalid	-	-	-	Invalid	-	-	1	0	1
Total									**1416**	**2387**	**3803**

[a] Symp = symptomatic, Asymp = asymptomatic.

[b] Infected (Urine), Non-Infected (Swabs).

Note: In the scenario where one or more of the sample types are invalid/not available (NA), for female subjects, the remaining sample types with valid results from NAAT1 and NAAT2 must have concordant positive or concordant negative results to determine the PIS as Infected or Not Infected, respectively. For all other cases where one or more of the sample types are invalid/not available (NA), the PIS is indeterminate.

Note: Female subjects with designated infection status (Infected or Non-Infected) and final valid **cobas**® CT/NG test results are considered evaluable and included in this summary table.

Note: cobas Invalid are the sum of instrument amplification/detection errors and samples excluded due to protocol deviations

Note: cobas Failed are hardware, software or operator errors causing no result reported

Note: + denotes Positive, - denotes Negative, NA denotes Not Available.

Note: UR = urine, VS = vaginal swab, PC = PreservCyt®, ES = endocervical swab.

Table 17: NG positive/negative analysis for male Patient Infected Status

	NAAT1[a]	NAAT2[a]	NAAT3[a]	cobas® CT/NG	Symptom Status[b]		
Patient Infected Status	**UR**	**UR**	**UR**	**UR**	**Symp**	**Asymp**	**Total**
Infected	+	+	+	+	81	5	86
Infected	NA	+	+	+	1	0	1
Total Infected					**82**	**5**	**87**
Non-Infected	-	-	-	-	215	863	1078
Non-Infected	+	-	-	-	2	7	9
Non-Infected	-	Invalid	-	-	3	2	5
Non-Infected	-	-	-	+	2	2	4
Non-Infected	Invalid	-	-	-	0	3	3
Non-Infected	-	-	Invalid	-	0	3	3
Non-Infected	-	+	-	+	1	1	2
Non-Infected	NA	-	-	-	0	1	1
Total Non-Infected					**223**	**882**	**1105***

[a] Symp = symptomatic, Asymp = asymptomatic.

*One subject was missing symptom status and is not included in this table.

Note: If at least 2 out of the 3 test results, for male subjects, are concordant positive or negative then the PIS can be considered as infected or non-infected, respectively. If one test result is invalid/not available (NA) and the other two test results are discordant then the PIS is indeterminate. If 2 or 3 test results are invalid/not available, then the PIS is indeterminate.

Note: Male subjects with designated patient infection status (Infected or Non-Infected) and final valid **cobas**® CT/NG test results are considered evaluable and included in this summary table.

Note: + denotes Positive, - denotes Negative, NA denotes Not Available.

Note: UR = urine.

Sensitivity, specificity, and predictive values of **cobas**® CT/NG for NG as defined by PIS are presented by gender, sample type, and symptom status in Table 18 (prospective fresh and archived specimens).

Table 18: NG clinical performance compared with Patient Infected Status by gender, sample type, and symptom status (prospective and archived prospectively collected specimens)

Sample Type[a]	Symptom Status[b]	Total (n)	SENS	95% Score CI	SPEC	95% Score CI	PREV (%)	PPV (%)	NPV (%)
Female									
UR (prospective)	Symp	1441	92.3% (24/26)	(75.9%, 97.9%)	99.8% (1412/1415)	(99.4%, 99.9%)	1.8	88.9	99.9
	Asymp	2418	87.1% (27/31)	(71.1%, 94.9%)	100.0% (2387/2387)	(99.8%, 100.0%)	1.3	100.0	99.8
	Overall	3859	89.5% (51/57) c	(78.9%, 95.1%)	99.9% (3799/3802)	(99.8%, 100.0%)	1.5	94.4	99.8
UR (archived)	Symp	94	100.0% (35/35)	(90.1%, 100.0%)	100.0% (59/59)	(93.9%, 100.0%)	37.2	100.0	100.0
	Asymp	101	97.6% (41/42)	(87.7%, 99.6%)	100.0% (59/59)	(93.9%, 100.0%)	41.6	100.0	98.3
	Overall	195	98.7% (76/77)	(93.0%, 99.8%)	100.0% (118/118)	(96.8%, 100.0%)	39.5	100.0	99.2
UR (prospective and archived)	Symp	1535	96.7% (59/61)	(88.8%, 99.1%)	99.8% (1471/1474)	(99.4%, 99.9%)	4.0	95.2	99.9
	Asymp	2519	93.2% (68/73)	(84.9%, 97.0%)	100.0% (2446/2446)	(99.8%, 100.0%)	2.9	100.0	99.8
	Overall	4054	94.8% (127/134)	(89.6%, 97.4%)	99.9% (3917/3920)	(99.8%, 100.0%)	3.3	97.7	99.8
VS-C	Symp	711	100.0% (11/11)	(74.1%, 100.0%)	99.7% (698/700)	(99.0%, 99.9%)	1.5	84.6	100.0
	Asymp	1225	100.0% (17/17)	(81.6%, 100.0%)	99.8% (1205/1208)	(99.3%, 99.9%)	1.4	85.0	100.0
	Overall	1936	100.0% (28/28)	(87.9%, 100.0%)	99.7% (1903/1908)	(99.4%, 99.9%)	1.4	84.8	100.0
VS-S	Symp	720	100.0% (14/14)	(78.5%, 100.0%)	99.7% (704/706)	(99.0%, 99.9%)	1.9	87.5	100.0
	Asymp	1187	100.0% (14/14)	(78.5%, 100.0%)	99.7% (1169/1173)	(99.1%, 99.9%)	1.2	77.8	100.0
	Overall	1907	100.0% (28/28)	(87.9%, 100.0%)	99.7% (1873/1879)	(99.3%, 99.9%)	1.5	82.4	100.0
PC (prospective)	Symp	1438	100.0% (25/25)	(86.7%, 100.0%)	99.9% (1412/1413)	(99.6%, 100.0%)	1.7	96.2	100.0
	Asymp	2413	93.5% (29/31)	(79.3%, 98.2%)	100.0% (2381/2382)	(99.8%, 100.0%)	1.3	96.7	99.9
	Overall	3851	96.4% (54/56)	(87.9%, 99.0%)	99.9% (3793/3795)	(99.8%, 100.0%)	1.5	96.4	99.9

Sample Type[a]	Symptom Status[b]	Total (n)	SENS	95% Score CI	SPEC	95% Score CI	PREV (%)	PPV (%)	NPV (%)
PC (archived)	Symp	48	95.7% (22/23)	(79.0%, 99.2%)	100.0% (25/25)	(86.7%, 100.0%)	47.9	100.0	96.2
	Asymp	23	100.0% (10/10)	(72.2%, 100.0%)	100.0% (13/13)	(77.2%, 100.0%)	43.5	100.0	100.0
	Overall	71	97.0% (32/33)	(84.7%, 99.5%)	100.0% (38/38)	(90.8%, 100.0%)	46.5	100.0	97.4
PC (prospective and archived)	Symp	1486	97.9% (47/48)	(89.1%, 99.6%)	99.9% (1437/1438)	(99.6%, 100.0%)	3.2	97.9	99.9
	Asymp	2436	95.1% (39/41)	(83.9%, 98.7%)	100.0% (2394/2395)	(99.8%, 100.0%)	1.7	97.5	99.9
	Overall	3922	96.6% (86/89)	(90.6%, 98.8%)	99.9% (3831/3833)	(99.8%, 100.0%)	2.3	97.7	99.9
ES (prospective)	Symp	1433	100.0% (24/24)	(86.2%, 100.0%)	99.9% (1408/1409)	(99.6%, 100.0%)	1.7	96.0	100.0
	Asymp	2410	90.3% (28/31)	(75.1%, 96.7%)	100.0% (2378/2379)	(99.8%, 100.0%)	1.3	96.6	99.9
	Overall	3843	94.5% (52/55)	(85.1%, 98.1%)	99.9% (3786/3788)	(99.8%, 100.0%)	1.4	96.3	99.9
ES (archived)	Symp	51	100.0% (21/21)	(84.5%, 100.0%)	100.0% (30/30)	(88.6%, 100.0%)	41.2	100.0	100.0
	Asymp	54	100.0% (24/24)	(86.2%, 100.0%)	100.0% (30/30)	(88.6%, 100.0%)	44.4	100.0	100.0
	Overall	105	100.0% (45/45)	(92.1%, 100.0%)	100.0% (60/60)	(94.0%, 100.0%)	42.9	100.0	100.0
ES (prospective and archived)	Symp	1484	100.0% (45/45)	(92.1%, 100.0%)	99.9% (1438/1439)	(99.6%, 100.0%)	3.0	97.8	100.0
	Asymp	2464	94.5% (52/55)	(85.1%, 98.1%)	100.0% (2408/2409)	(99.8%, 100.0%)	2.2	98.1	99.9
	Overall	3948	97.0% (97/100)	(91.5%, 99.0%)	99.9% (3846/3848)	(99.8%, 100.0%)	2.5	98.0	99.9
Male									
UR	Symp	305	100.0% (82/82)	(95.5%, 100.0%)	98.7% (220/223)	(96.1%, 99.5%)	26.9	96.5	100.0
	Asymp	887	100.0% (5/5)	(56.6%, 100.0%)	99.7% (879/882)	(99.0%, 99.9%)	0.6	62.5	100.0
	Overall	1192*	100.0% (87/87)	(95.8%, 100.0%)	99.5% (1099/1105)	(98.8%, 99.8%)	7.3	93.5	100.0

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

[a] UR = urine, VS-C = clinician-collected vaginal swab, VS-S = self-collected vaginal swab, PC = PreservCyt®, ES = endocervical swab.

[b] Symp = symptomatic, Asymp = asymptomatic.

[c] Five NG PIS infected females had a NG negative urine specimen with NAAT1 and NAAT2 while they had a NG positive vaginal swab with NAAT1 and NAAT2

* One subject was missing symptom status and is not included in this table.

Note: In the scenario where one or more of the sample types are invalid/not available, for female subjects, the remaining sample types with valid results from NAAT1 and NAAT2 must have concordant positive or concordant negative results to determine the PIS as Infected or Non-Infected, respectively. For all other cases where one or more of the sample types are invalid/ not available, the PIS is indeterminate.

Note: If at least 2 out of the 3 test results, for male subjects, are concordant positive or negative then the PIS can be considered as Infected or Non-Infected, respectively. If one test result is invalid/not available and the other two test results are discordant then the PIS is indeterminate. If 2 or 3 test results are invalid/not available, then the PIS is indeterminate.

Note: Subjects with designated patient infection status (Infected or Non-Infected) and final valid **cobas**® CT/NG test results are considered evaluable and included in this summary table. An evaluable subject may not have all available sample types or valid test results.

Note: Archived prospectively collected specimens were from COB-CTNG-282 study and included female PIS positive subjects that have available sample with adequate volume for testing.

Note: CI = confidence interval, PREV = prevalence, SENS = sensitivity, SPEC = specificity, PPV = positive predictive value, NPV = negative predictive value.

5.2. Clinical Reproducibility

5.2.1. Study Design

A Reproducibility Study was performed across different sites, lots, operators/batches days, for **cobas**® CT/NG using three panels prepared from swabs and urine in **cobas**® PCR Media and cervical specimens in PreservCyt® Solution. PCR testing was performed at two external sites and one site that was in-house at Roche Molecular Systems. One panel consisted of the three sample matrices, with six concentrations per matrix, and three replicates per concentration for a total of 54 samples in one panel. A batch was comprised of one 54-sample panel and two controls (one positive control and one negative control). Two operators at each site tested one batch each per day. Two valid batches had to be completed within a 24-hour period. Each site received two of three reagent lots and performed 6 days of testing per reagent lot for a total of 12 days of testing.

5.2.2. Results

The Reproducibility Study was executed with a total of 3,888 tests performed on the 6 panel groups, consisting of 1,296 tests for each panel type (urine, swab, and PreservCyt®), with only two failed tests each from PreservCyt®. No false positive results for either CT or NG were observed in the three panel types for negative panel members; thus the negative percent agreement was 100% for each analyte. Results for the positive panel members were highly reproducible across different lots, sites/instruments, days and operators/batches.

5.2.2.1. Negative panel results

For each sample type, all of the 216 valid tests from the negative panel members resulted in "Negative Results". Hence, for both CT and NG, the percent of correct results (analytical specificity) was estimated as 100% with a corresponding 95% exact confidence interval of 98.3%, 100% for **cobas**® PCR Media/urine, for **cobas**® PCR Media/swab and for PreservCyt®/cervical sample types.

5.2.2.2. Chlamydia trachomatis results

For each positive panel member, precision was evaluated using a random effects model by sample type with terms for lot, site, day, operator/batch within site, lot and day, and within-batch components on the corresponding analyte cycle threshold (Ct) values of **cobas**® CT/NG. Table 19 presents the total SD, and total percent CV (%) from these analyses for each panel type, respectively. The range of the total coefficient of variation, among positive panel members, was from 0.9% to 3.2%. The maximum total coefficient of variation was observed in the lowest concentration of positive panel members (0.3x LoD CT, 0.3x LoD NG) and most of that variability (98.6% for urine, 100% for swab and 81.7% for cervical) was explained by random error (within-batch).

Table 19: CT: overall mean, attributable percentage of total variance, total precision standard deviation, and CV(%) of cobas® CT/NG cycle threshold (Ct) values by CT positive panel member for each media type

Panel Member		Mean CT value		Percentage of Total Variance (CV[%])					Total Precision	
Media Type	Concen-tration	N [a]	Mean Estimate [b]	Site	Lot	Day	Operator /Batch	Within-Batch	SD [c]	CV(%) [d]
PCR Media/ Urine	0.3xLOD CT, 0.3xLOD NG	154	39.2	1.4% (0.4)	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	98.6% (3.0)	1.20	3.1
	1xLOD CT, Negative NG	216	36.8	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	100.0% (1.5)	0.54	1.5
	3xLOD CT, 1xLOD NG	216	35.4	2.4% (0.1)	0.0% (0.0)	21.1% (0.4)	0.0% (0.0)	76.5% (0.8)	0.33	0.9
	1xLOD CT, 3xLOD NG	216	36.9	0.0% (0.0)	0.0% (0.0)	10.3% (0.5)	4.4% (0.3)	85.3% (1.5)	0.59	1.6
PCR Media/ Swab	0.3xLOD CT, 0.3xLOD NG	128	39.5	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	100.0% (3.2)	1.26	3.2
	1xLOD CT, Negative NG	216	37.2	0.0% (0.0)	1.6% (0.2)	6.6% (0.5)	0.0% (0.0)	91.8% (1.7)	0.66	1.8
	3xLOD CT, 1xLOD NG	216	35.5	4.7% (0.2)	0.0% (0.0)	9.0% (0.3)	4.8% (0.2)	81.6% (0.9)	0.37	1.0
	1xLOD CT, 3xLOD NG	216	37.2	0.0% (0.0)	0.0% (0.0)	3.6% (0.4)	0.0% (0.0)	96.4% (2.3)	0.87	2.3
PreservCyt/ Cervical	0.3xLOD CT, 0.3xLOD NG	92	39.9	0.0% (0.0)	0.0% (0.0)	18.3% (1.4)	0.0% (0.0)	81.7% (2.9)	1.29	3.2
	1xLOD CT, Negative NG	216	37.0	12.0% (0.6)	1.9% (0.2)	0.0% (0.0)	0.0% (0.0)	86.2% (1.5)	0.60	1.6
	3xLOD CT, 1xLOD NG	216	35.6	0.6% (0.1)	3.7% (0.2)	0.0% (0.0)	6.3% (0.3)	89.3% (0.9)	0.36	1.0
	1xLOD CT, 3xLOD NG	214	36.8	13.1% (0.6)	3.7% (0.3)	5.3% (0.4)	2.3% (0.3)	75.6% (1.5)	0.63	1.7

Note: The table only includes results with detectable analyte. SD = standard deviation. CV(%) = percent coefficient of variation.

[a] Number of valid tests with detectable analyte.

[b] Calculated using SAS MIXED procedure.

[c] Calculated using the total variability from the SAS MIXED procedure.

[d] CV(%) = (SD/Mean) * 100.

LOD= Limit of Detection; CT= Chlamydia trachomatis ; NG = Neisseria gonorrhoeae.

Table 20 through Table 22 present the percent agreement of CT test results for panel members by lot, site, and day for each media type, respectively.

Table 20: CT: Percent agreement by panel member for lot, site and day - cobas® PCR Media/urine

			CT Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
Negative CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
0.3x LoD CT, 0.3x LoD NG	1.20	3.1	1	76.4	55/72	1	68.1	49/72	1	80.6	29/36
			2	70.8	51/72	2	73.6	53/72	2	77.8	28/36
			3	66.7	48/72	3	72.2	52/72	3	66.7	24/36
									4	77.8	28/36
									5	69.4	25/36
									6	55.6	20/36
1x LoD CT, Negative NG	0.54	1.5	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
Negative CT, 1x LoD NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36

			CT Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
3x LoD CT, 1x LoD NG	0.33	0.9	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
1x LoD CT, 3x LoD NG	0.59	1.6	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36

[a] For CT Negative samples, Percent Agreement = (number of CT negative results/total valid results) x 100.
For CT Positive samples, Percent Agreement = (number of CT positive results/total valid results) x 100.
[b] Site 1, Site 2, and Site 3, respectively.
Ct=Cycle threshold; SD=Standard Deviation; CV=Coefficient of Variation; LoD= Limit of Detection.
CT= *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; n/a= not applicable.

Table 21: CT: Percent agreement by panel member for lot, site and day - cobas® PCR Media/swab

			CT Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
Negative CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
0.3x LoD CT, 0.3x LoD NG	1.26	3.2	1	61.1	44/72	1	56.9	41/72	1	50.0	18/36
			2	59.7	43/72	2	61.1	44/72	2	63.9	23/36
			3	56.9	41/72	3	59.7	43/72	3	55.6	20/36
									4	61.1	22/36
									5	66.7	24/36
									6	58.3	21/36

			CT Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
1x LoD CT, Negative NG	0.66	1.8	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
Negative CT, 1x LoD NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
3x LoD CT, 1x LoD NG	0.37	1.0	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
1x LoD CT, 3x LoD NG	0.87	2.3	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36

[a] For CT Negative samples, Percent Agreement = (number of CT negative results/total valid results) x 100.
For CT Positive samples, Percent Agreement = (number of CT positive results/total valid results) x 100.

[b] Site 1, Site 2, and Site 3, respectively.

Ct=Cycle threshold; SD=Standard Deviation; CV=Coefficient of Variation; LoD= Limit of Detection.
CT= *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; n/a= not applicable.

Table 22: CT: Percent agreement by panel member for lot, site and day - PreservCyt®/cervical

	CT Percent Agreement[a]

Panel Member	Ct SD	Ct CV %	Lot			Site[b]			Day		
Negative CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
0.3x LoD CT, 0.3x LoD NG	1.29	3.2	1	38.9	28/72	1	34.7	25/72	1	40.0	14/35
			2	47.9	34/71	2	48.6	35/72	2	52.8	19/36
			3	41.7	30/72	3	45.1	32/71	3	38.9	14/36
									4	47.2	17/36
									5	41.7	15/36
									6	36.1	13/36
1x LoD CT, Negative NG	0.60	1.6	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
Negative CT, 1x LoD NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
3x LoD CT, 1x LoD NG	0.36	1.0	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
1x LoD CT, 3x LoD NG	0.63	1.7	1	98.6	71/72	1	98.6	71/72	1	97.2	35/36
			2	100.0	71/71	2	100.0	71/71	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36

			CT Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
									4	100.0	35/35
									5	100.0	36/36
									6	100.0	36/36

[a] For CT Negative samples, Percent Agreement = (number of CT negative results/total valid results) x 100.
For CT Positive samples, Percent Agreement = (number of CT positive results/total valid results) x 100.
[b] Site 1, Site 2, and Site 3, respectively.
Ct=Cycle threshold; SD=Standard Deviation; CV=Coefficient of Variation; LoD= Limit of Detection.
CT= *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; n/a= not applicable.

5.2.2.3. Neisseria gonorrhoeae results

Analysis of variance components of the Ct values from valid NG test results were performed on positive panel members. Table 23 presents the total SD and total CV (%) from these analyses. The range of the total coefficient of variation, among positive panel members, was from 1.0% to 3.1%. The maximum total coefficient of variation was observed in the lowest concentration of positive panel members (0.3x LoD CT, 0.3x LoD NG) and most of that variability (98.7% for urine, 98.1% for swab and 85.3% for cervical) was explained by random error (within-batch).

Table 23: NG: overall mean, attributable percentage of total variance, total precision standard deviation, and CV(%) of cobas® CTNG cycle threshold (Ct) values by NG positive panel member for each media type

Panel Member		Mean CT value		Percentage of Total Variance (CV[%])					Total Precision	
Media Type	Concen-tration	N [a]	Mean Estimate [b]	Site	Lot	Day	Operator /Batch	Within-Batch	SD [c]	CV(%) [d]
PCR Media/ Urine	0.3xLOD CT, 0.3xLOD NG	159	39.3	0.7% (0.3)	0.0% (0.0)	0.6% (0.2)	0.0% (0.0)	98.7% (3.0)	1.20	3.0
	Negative CT, 1xLOD NG	216	36.7	0.0% (0.0)	0.5% (0.1)	6.9% (0.5)	0.0% (0.0)	92.6% (1.7)	0.63	1.7
	3xLOD CT, 1xLOD NG	216	36.6	0.0% (0.0)	2.5% (0.3)	8.3% (0.5)	0.0% (0.0)	89.2% (1.6)	0.61	1.7
	1xLOD CT, 3xLOD NG	216	35.1	0.0% (0.0)	0.0% (0.0)	14.0% (0.4)	0.0% (0.0)	86.0% (1.0)	0.37	1.0
PCR Media/ Swab	0.3xLOD CT, 0.3xLOD NG	113	39.8	0.0% (0.0)	0.0% (0.0)	1.9% (0.4)	0.0% (0.0)	98.1% (3.1)	1.25	3.1
	Negative CT, 1xLOD NG	212	38.2	0.0% (0.0)	0.1% (0.1)	1.8% (0.4)	6.5% (0.7)	91.6% (2.6)	1.04	2.7
	3xLOD CT, 1xLOD NG	216	36.9	0.0% (0.0)	0.0% (0.0)	6.3% (0.6)	0.0% (0.0)	93.7% (2.1)	0.82	2.2
	1xLOD CT, 3xLOD NG	216	35.7	0.0% (0.0)	3.8% (0.3)	14.4% (0.5)	0.0% (0.0)	81.8% (1.3)	0.50	1.4
PreservCyt/ Cervical	0.3xLOD CT, 0.3xLOD NG	112	39.5	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	14.7% (1.0)	85.3% (2.4)	1.04	2.6
	Negative CT, 1xLOD NG	216	35.7	7.2% (0.4)	4.9% (0.3)	0.0% (0.0)	0.0% (0.0)	87.9% (1.3)	0.49	1.4
	3xLOD CT, 1xLOD NG	216	36.3	0.0% (0.0)	0.0% (0.0)	0.0% (0.0)	9.6% (0.5)	90.4% (1.6)	0.61	1.7
	1xLOD CT, 3xLOD NG	215	34.6	2.3% (0.2)	0.0% (0.0)	5.8% (0.2)	12.0% (0.3)	79.8% (0.9)	0.34	1.0

Note: The table only includes results with detectable analyte. SD = standard deviation. CV(%) = percent coefficient of variation.
[a] Number of valid tests with detectable analyte.
[b] Calculated using SAS MIXED procedure.
[c] Calculated using the total variability from the SAS MIXED procedure.
[d] CV(%) = (SD/Mean) * 100.
LOD= Limit of Detection; CT = Chlamydia trachomatis ; NG = Neisseria gonorrhoeae.

Table 24 through Table 26 present the percent agreement of NG test results for panel members by lot, site, and day for each media type, respectively.

Table 24: NG: Percent agreement by panel member for lot, site and day - cobas® PCR Media/urine

			NG Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
Negative CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
0.3x LoD CT, 0.3x LoD NG	1.20	3.0	1	79.2	57/72	1	70.8	51/72	1	77.8	28/36
			2	73.6	53/72	2	76.4	55/72	2	75.0	27/36
			3	68.1	49/72	3	73.6	53/72	3	72.2	26/36
									4	80.6	29/36
									5	61.1	22/36
									6	75.0	27/36
1x LoD CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
Negative CT, 1x LoD NG	0.63	1.7	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
3x LoD CT, 1x LoD NG	0.61	1.7	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36

			NG Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
1x LoD CT, 3x LoD NG	0.37	1.0	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36

[a] For NG Negative samples, Percent Agreement = (number of NG negative results/total valid results) x 100.

For NG Positive samples, Percent Agreement = (number of NG positive results/total valid results) x 100.

[b] Site 1, Site 2, and Site 3, respectively.

Ct=Cycle threshold; SD=Standard Deviation; CV=Coefficient of Variation; LoD= Limit of Detection.

CT= *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; n/a= not applicable.

Table 25: NG: Percent agreement by panel member for lot, site and day - cobas® PCR Media/swab

			NG Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
Negative CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
0.3x LoD CT, 0.3x LoD NG	1.25	3.1	1	50.0	36/72	1	50.0	36/72	1	52.8	19/36
			2	51.4	37/72	2	52.8	38/72	2	55.6	20/36
			3	55.6	40/72	3	54.2	39/72	3	44.4	16/36
									4	55.6	20/36
									5	52.8	19/36
									6	52.8	19/36

			NG Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
1x LoD CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
Negative CT, 1x LoD NG	1.04	2.7	1	100.0	72/72	1	97.2	70/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	94.4	68/72	3	97.2	70/72	3	97.2	35/36
									4	100.0	36/36
									5	97.2	35/36
									6	94.4	34/36
3x LoD CT, 1x LoD NG	0.82	2.2	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
1x LoD CT, 3x LoD NG	0.50	1.4	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36

[a] For NG Negative samples, Percent Agreement = (number of NG negative results/total valid results) x 100.
For NG Positive samples, Percent Agreement = (number of NG positive results/total valid results) x 100.

[b] Site 1, Site 2, and Site 3, respectively.

Ct=Cycle threshold; SD=Standard Deviation; CV=Coefficient of Variation; LoD= Limit of Detection.

CT= *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; n/a= not applicable.

Table 26: NG: Percent agreement by panel member for lot, site and day - PreservCyt®/cervical

			NG Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
Negative CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
0.3x LoD CT, 0.3x LoD NG	1.04	2.6	1	63.9	46/72	1	59.7	43/72	1	54.3	19/35
			2	47.9	34/71	2	52.8	38/72	2	55.6	20/36
			3	44.4	32/72	3	43.7	31/71	3	47.2	17/36
									4	55.6	20/36
									5	52.8	19/36
									6	47.2	17/36
1x LoD CT, Negative NG	n/a	n/a	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
Negative CT, 1x LoD NG	0.49	1.4	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36
3x LoD CT, 1x LoD NG	0.61	1.7	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	72/72	2	100.0	72/72	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	36/36
									5	100.0	36/36
									6	100.0	36/36

			NG Percent Agreement[a]								
Panel Member	**Ct SD**	**Ct CV %**	**Lot**			**Site[b]**			**Day**		
1x LoD CT, 3x LoD NG	0.34	1.0	1	100.0	72/72	1	100.0	72/72	1	100.0	36/36
			2	100.0	71/71	2	100.0	71/71	2	100.0	36/36
			3	100.0	72/72	3	100.0	72/72	3	100.0	36/36
									4	100.0	35/35
									5	100.0	36/36
									6	100.0	36/36

[a] For NG Negative samples, Percent Agreement = (number of NG negative results/total valid results) x 100.
For NG Positive samples, Percent Agreement = (number of NG positive results/total valid results) x 100.
[b] Site 1, Site 2, and Site 3, respectively.
Ct=Cycle threshold; SD=Standard Deviation; CV=Coefficient of Variation; LoD= Limit of Detection.
CT= *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; n/a= not applicable.

5.2.2.4. Percentage agreement results

Table 27 shows the percent agreement for each target (CT, NG) with the associated 95% Exact CI.

Table 27: Percent agreement for panel members with concentration at or near the LoD (1x LoD) or 3x LoD

		CT		NG	
Media Type	**Panel Member**	**Percent Agreement**	**Percent Agreement 95% Exact CI**	**Percent Agreement**	**Percent Agreement 95% Exact CI**
PCR Media/Urine	1.0x LoD CT, Negative NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	Negative CT, 1.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	3.0x LoD CT, 1.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	1.0x LoD CT, 3.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
PCR Media/Swab	1.0x LoD CT, Negative NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	Negative CT, 1.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	98.1 (212/216)	(95.3, 99.5)
	3.0x LoD CT, 1.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	1.0x LoD CT, 3.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
PreservCyt®/ Cervical	1.0x LoD CT, Negative NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	Negative CT, 1.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	3.0x LoD CT, 1.0x LoD NG	100.0 (216/216)	(98.3, 100.0)	100.0 (216/216)	(98.3, 100.0)
	1.0x LoD CT, 3.0x LoD NG	99.5 (214/215)	(97.4, 100.0)	100.0 (215/215)	(98.3, 100.0)

Notes: LoD= Limit of Detection; CT= *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*.

For panel members with concentrations at or near the limit of detection (e.g., 1x LoD) of the test, the lower limit of the 2-sided 95% exact CI of the percentage of correct test results should be equal to or greater than 91%.

For panel members with concentrations 3-times above the limit of detection (e.g., 3x LoD) of the test, the lower limit of the 2-sided 95% exact CI of the percentage of correct test results should be equal to or greater than 98%.

For panel members with concentrations at or near the limit of detection (e.g., 1x LoD) of the test, the lower limit of the 2-sided 95% exact CI of the percentage of correct test results was at least 97.4% for CT and 95.3% for NG.

For panel members with concentrations 3-times above the limit of detection (e.g., 3x LoD) of the test, the lower limit of the 2-sided 95% exact CI of the percentage of correct test results was 98.3% for both CT and NG.

6. CONCLUSIONS

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