cobas® CT/NG Test
510(k) Summary

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Contact:	James Bonds
Date of Preparation:	January 24, 2012
Device Trade Name:	**cobas**® CT/NG Test
Common Name:	*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (NG) Test
Type of Test:	Nucleic Acid Amplification Test, DNA, *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (NG), qualitative
Classification Names:	Chlamydia serological reagents Neisseria spp. Direct serological test reagents Real Time Nucleic Acid Amplification System
Regulations:	866.3120 866.3390 862.2570
Product codes:	MKZ (DNA Probe, Nucleic Acid Amplification, Chlamydia) LSL (DNA Reagents, Neisseria) OOI (Real Time Nucleic Acid Amplification System)
Panel:	Microbiology
Predicate Devices - Assay:	Gen-Probe APTIMA Combo 2 Assay (K060652) BD ProbeTec Q^{x} *Chlamydia trachomatis* Amplified DNA Assay (K091724) and BD ProbeTec Q^{x} *Neisseria gonorrhoeae* Amplified DNA Assay (K091730)
Predicate Device – Collection Kits	Abbott *m*ulti-Collect Specimen Collection Kit (K092704)

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1. DEVICE DESCRIPTION

The Roche Molecular Systems (RMS) **cobas**® CT/NG Test consists of five reagent kits:

- **cobas**® 4800 System Sample Preparation Kit
- **cobas**® 4800 CT/NG Amplification/Detection Kit
- **cobas**® 4800 CT/NG Controls Kit
- **cobas**® 4800 System Wash Buffer Kit
- **cobas**® 4800 System Control Diluent Kit

Sample Collection Kits to be used for the cobas® CT/NG Test are:

- **cobas**® PCR Female Swab Sample Kit
- **cobas**® PCR Urine Sample Kit

The **cobas**® CT/NG Test for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) is based on two major processes: (1) automated sample preparation to obtain nucleic acids, including CT and NG DNA; (2) simultaneous PCR amplification of target DNA sequences using both CT and NG specific complementary primer pairs and real-time detection of cleaved fluorescent-labeled CT and NG specific oligonucleotide detection probes. Internal control, containing CT and NG DNA, is added to all samples during automated sample preparation and is amplified and detected simultaneously with each sample to monitor the entire process.

The **cobas**® 4800 System utilizes the **cobas x** 480 Instrument for automated sample preparation, and the automated **cobas z** 480 Analyzer for automated amplification and detection.
The **cobas**® 4800 system software integrates the sample preparation with nucleic acid amplification and detection to generate test results.

2. INTENDED USE

Assay

The **cobas**® CT/NG Test is an *in vitro* nucleic acid amplification test that utilizes Polymerase Chain Reaction (PCR) and nucleic acid hybridization for the qualitative detection of *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae (NG)* DNA to aid in the diagnosis of chlamydial and gonococcal disease. The test may be used with vaginal swab specimens self-collected in a clinical setting and male urine from both symptomatic and asymptomatic individuals. Specimens to be tested should be collected in **cobas**® PCR Media.

Ancillary Collection Kits

The **cobas**® PCR Female Swab Sample Kit is used to collect and transport self-collected vaginal swab specimens in a clinical setting. 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 Test. **NOTE: This collection kit should not be used for collection of alternative gynecological specimens.**

The **cobas**® PCR Urine Sample Kit is used to collect and transport male 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 Test. **NOTE: This collection kit should not be used for collection of female urine specimens.**

3. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the RMS **cobas**® CT/NG Test 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 RMS **cobas**® CT/NG Test is substantially equivalent to significant characteristics of the identified predicate devices, the Gen-Probe APTIMA Combo 2 Assay (K060652), the BD ProbeTec Q^{x} *Chlamydia trachomatis* Amplified DNA Assay (K091724) and the BD ProbeTec Q^{x} *Neisseria gonorrhoeae* Amplified DNA Assay (K091730).

Table 1: Comparison of the cobas® CT/NG Test with the Predicate Devices

	Submitted Device: RMS cobas® CT/NG Test	**Predicate Device: Gen-Probe APTIMA Combo 2 Assay (K060652)**	**Predicate Devices: BD ProbeTec Q^x *CT* Amplified DNA Assay (K091724) and BD ProbeTec Q^x GC Amplified DNA Assay (K091730)**
General Intended Use	Qualitative *in vitro* diagnostic test for the direct qualitative detection of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* in patient specimens	same	same
Sample Types	Male urine Patient-collected vaginal swabs	Male urine Male urethral swabs Female urine Endocervical swabs Clinician-collected vaginal swabs Patient-collected vaginal swabs Cervical specimens in PreservCyt® media	Male urine Male urethral swabs Female urine Endocervical swabs Patient-collected vaginal swabs Cervical specimens in PreservCyt® and SurePath® media
Subject Status	Asymptomatic and symptomatic	Asymptomatic and symptomatic	Asymptomatic and symptomatic
Sample Collection Devices	Urine collection kit Swab collection kit	Urine collection kit Swab collection kit	Urine collection kit Vaginal collection kit
CT Analyte Targets	CT cryptic plasmid DNA CT *ompA* gene	CT ribosomal RNA	CT cryptic plasmid DNA
NG Analyte Targets	NG genomic DNA	NG ribosomal RNA	NG genomic DNA
Sample Preparation Procedure	Semi-automated	Semi-automated/automated	Manual/semi-automated
Amplification Technology	Real-time PCR	Ribosomal RNA transcription medicated amplification (TMA)	Strand displacement DNA amplification (SDA)
Detection Chemistry	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)	Photon measurment from selectively hybridized chemiluninescent probes reported as Relative Light Units (RLU)	Fluorescent dye labeled probes using fluorescence resonance energy transfer (FRET)

	Submitted Device: RMS cobas® CT/NG Test	**Predicate Device: Gen-Probe APTIMA Combo 2 Assay (K060652)**	**Predicate Devices: BD ProbeTec Q^x *CT* Amplified DNA Assay (K091724) and BD ProbeTec Q^x GC Amplified DNA Assay (K091730)**
Result Analysis	Based on PCR cycle threshold (Ct) analysis	Determined by a cut-off based on the total RLU and kinetic curve type	Determined by relating MOTA scores (signal strength) to pre-determined cutoff values

As indicated in Table 2, the **cobas®** PCR Female Swab Sample Kit and the **cobas®** PCR Urine Sample Kit are substantially equivalent to those characteristics for the predicate device. The collection kits have the same basic components and intended use, and all are intended as accessories to their respective assays. Data presented in this pre-market notification further support the substantial equivalence of the subject devices to the predicate.

Table 2: Comparison of the cobas® PCR Sample Collection Devices with the Predicate Device

	Submitted Device: RMS cobas® PCR Female Swab Sample Kit	**Submitted Device: RMS cobas® PCR Urine Sample Kit**	**Predicate Device: Abbott *m*ulti-Collect Specimen Collection Kit (K092704)**
General Intended Use	Collection and transport of vaginal swab specimens self-collected in a clinical environment for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* per the instructions provided. Not intended for home use.	Collection and transport of urine specimens for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* per the instructions provided. Not intended for home use.	Collection and transport of male and female, swab and urine specimens for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* per instructions provided. Not intended for home use.
Sample Types	Vaginal swab self-collected in a clinical setting	Male urine	Male urine Male urethral swabs Female urine Endocervical swabs Vaginal swabs, clinician collected and self-collected

In summary, the intended use, technology, and functionality of the **cobas®** CT/NG Test as compared to the predicate devices do not raise any new types of safety or effectiveness questions and are substantially equivalent.

4. NON-CLINICAL PERFORMANCE EVALUATION

4.1. Analytical Sensitivity

The analytical sensitivity (Limit of Detection or LOD) for the **cobas®** CT/NG Test was determined by analyzing dilutions of quantified CT and NG cultures. Cultures of CT and NG were diluted into negative vaginal swab specimen in **cobas®** PCR Media and negative urine specimen plus **cobas®** PCR Media to determine the LOD for vaginal swab and urine specimens, respectively. All levels were analyzed using the full **cobas®** CT/NG Test workflow across 3 unique lots of **cobas®** CT/NG Test reagents. This test defines LOD as the target concentration which can be detected as positive in ≥ 95% of the replicates tested with each reagent lot.

The LOD for the CT serovar D culture and NG strain 19424 in **cobas®** PCR Media, vaginal swab specimens stabilized in **cobas®** PCR Media and urine specimens diluted into **cobas®** PCR Media are shown in Table 3.

Table 3: cobas® CT/NG Test Limit of Detection

Specimen Types	*C. trachomatis*			*N. gonorrhoeae*		
	Levels Tested	Replicates/ Level	LOD (IFU/mL)	Levels Tested	Replicates/ Level	LOD (CFU/mL)
Urine	7	192*	0.75	7	192*	2.25
Vaginal Swabs	5	192**	10.00	5	192**	100.00

*Testing included one negative level with 167-168 replicates

**Testing included one negative level with 82-84 replicates

4.2. Inclusivity

The sensitivity of the **cobas®** CT/NG Test was determined for 14 additional CT serovars, the Swedish new variant (nvCT) strain and an additional 44 independently isolated strains of NG. Testing was done to demonstrate that these targets can be detected around the LOD levels determined during analytical sensitivity testing for the CT serovar D culture and NG strain

19424. Panels were prepared as described for the LOD study with the number of panel levels varying from 1 to 5, as required. At least 49 replicates were tested for each panel level using one lot of **cobas**®CT/NG Test reagents. Results are shown in Table 4 and Table 5. In Table 5, all NG strains with identical LOD results are presented as a group, shown in the columns labeled "Numbers of NG Strains." Since LOD evaluation was done with samples stabilized in **cobas**® PCR Media, the LOD for untreated urine is twice the level reported in Table 4 and Table 5.

The analytical sensitivity for all 14 CT serovars plus the nvCT variant (Table 4) ranged from 0.2 IFU/mL (IFU= Inclusion Forming Units) to 5.0 IFU/mL in **cobas**® PCR Media and from 0.13 IFU/mL to 0.75 IFU/mL in **cobas**® PCR Media plus negative urine specimen. All CT serovars and the nvCT variant were tested at 10 IFU/mL only in stabilized negative vaginal specimen and all showed 100% positive hit rates at 10 IFU/mL.

The analytical sensitivity for all 44 NG strains ranged from 3.0 CFU/mL to 20 CFU/mL in **cobas**® PCR Media and was 3.75 CFU/mL in **cobas**® PCR Media plus urine specimens. All NG strains were tested at 100 CFU/mL only in stabilized negative vaginal specimen. All showed 100% hit rates at 100 CFU/mL (CFU = Colony Forming Units).

Table 4: Summary of CT Serovars/Variant Inclusivity Verification Results

Serovar Type or Variant	LOD Results for *C. trachomatis*			
	Vaginal Swabs*		Urine	
	IFU/mL	% Pos	IFU/mL	% Pos
A	10.0	100%	0.125	98%
B	10.0	100%	0.75	100%
Ba	10.0	100%	0.75	100%
C	10.0	100%	0.75	100%
E	10.0	100%	0.75	100%
F	10.0	100%	0.75	100%
G	10.0	100%	0.75	100%
H	10.0	100%	0.75	100%
I	10.0	100%	0.75	98%
J	10.0	100%	0.125	96%
K	10.0	100%	0.75	100%
LV Type 1	10.0	100%	0.125	100%

LV Type 2	10.0	100%	0.125	100%
LV Type 3	10.0	100%	0.125	100%
nvCT	10.0	100%	0.75	100%

Table 5: Summary of NG Strains Inclusivity Verification Results

Numbers of NG Strains	**LOD Urine**	
	CFU/mL	**% Hit Rate**
3	3.75	96%
4	3.75	98%
37	3.75	100%
Total = 44		
Numbers of NG Strains	**LOD Vaginal Swabs***	
	CFU/mL	**% Hit Rate**
Total = 44	100	100%

4.3. Competitive Inhibition

Panels were prepared by spiking CT and NG cultures into urine and vaginal specimens stabilized in **cobas**® PCR Media to various concentration levels to examine the potential for competitive inhibition. Panels were prepared with two strains each of CT and NG. Panels were tested in one run per day over the course of 5 days. Two replicates of each panel member were tested in every run, generating a maximum of 10 test results for each level and CT and NG strain respectively. Average Ct values for each of the panel levels are summarized in Tables 6 and 7. All CT and NG hit rates were 100% for all panel levels in both matrices. Competitive inhibition was not seen in any combination of CT and NG levels in either matrix.

Table 6: Competitive inhibition Study for CT and NG Cultures in Urine Stabilized in cobas® PCR Media (Ct Values)

Panel Level		Strain 1		Strain 2	
CT Level / IFU/mL	NG Level / (CFU/mL)	CT	NG	CT	NG
Low/2	Low/6	35.1	34.8	32.5	34.8
Low/2	Medium/ 24	34.9	33.1	32.6	33.0
Medium/ 8	Low/6	33.5	34.1	30.1	35.0

High/ 1.00E+05	Low/6	19.4	34.1	18.6	35.0
Low/2	High/ 1.00E+06	35.2	17.6	32.6	17.4
High/ 1.00E+05	High/ 1.00E+06	19.5	18.1	18.9	17.7

Table 7: Competitive inhibition Study for CT and NG Cultures in Vaginal Swabs Collected in cobas® PCR Media (Ct Values)

Panel Level		Strain 1		Strain 2	
CT Level/ IFU/mL	NG Level / (CFU/mL)	CT	NG	CT	NG
Low/25	Low/250	36.4	35.1	34.1	34.7
Low/25	Medium/ 1000	36.2	33.2	33.7	31.8
Medium/ 100	Low/250	34.5	35.1	32.2	34.4
High/ 1.00E+05	Low/250	23.9	33.8	22.9	33.8
Low/25	High/ 1.00E+06	35.7	22.8	33.8	22.0
High/ 1.00E+05	High/ 1.00E+06	23.7	23.2	21.9	22.1

4.4. Analytical Specificity

A panel of 184 bacteria, fungi and viruses, including those commonly found in the male/female urogenital tract, as well as representatives of *N. cineria, N. flava, N. lactamica, N. perflava* and *N. subflava* and other phylogenetically related organisms, were tested with the **cobas®** CT/NG Test to assess analytical specificity. The organisms listed in Table 6 were spiked at high concentrations (microorganisms tested below 1 x 10^6 copies/mL are listed in Table 9) into CT/NG negative urine specimens plus **cobas®** PCR Media and pooled negative vaginal specimen spiked with CT and NG cultures at 3 times the limit of detection.

Results indicated that none of these organisms interfered with detection of CT and NG or produced a false positive result in the CT/NG negative matrices.

Table 8: Microorganisms Tested for Analytical Specificity

Achromobacter xerosis	*Helicobacter pylori*	*Neisseria sicca*
Acinetobacter calcoaceticus	Hepatitis B virus (HBV)	*Neisseria subflava*
Acinetobacter lwoffi	Hepatitis C virus (HCV)	*Neisseria subflava 6458*
Acinetobacter sp. genospecies 3	Human immunodeficiency virus	*Neisseria subflava 6617*

Actinomyces israelii	Human papillomavirus type 16 (CaSki cells)	*Neisseria subflava 6618*
Actinomyces pyogenes	Human papillomavirus type 18 (HeLa cells)	*Neisseria subflava 7441*
Adenovirus	Herpes Simplex Virus (HSV-1)	*Neisseria subflava 7452*
Aerococcus viridans	Herpes Simplex Virus (HSV-2)	*Neisseria weaverii*
Aeromonas hydrophila	*Kingella dentrificans*	*Pantoea agglomerans*
Alcaligenes faecalis	*Kingella kingae*	*Paracoccus denitrificans*
Bacillus subtilis	*Klebsiella oxytoca*	*Pasteurella maltocida*
Bacillus thuringiensis	*Klebsiella pneumoniae ss ozaenae*	*Pediococcus acidilactica*
Bacteroides caccae	*Lactobacillus acidophillus*	*Peptostreptococcus anaerobius*
Bacteroides fragilis	*Lactobacillus brevis*	*Peptostreptococcus asacharolyticus*
Bacteroides ureolyticus	*Lactobacillus crispatus*	*Peptostreptococcus magnus*
Bifidobacterium adolescentis	*Lactobacillus delbrueckii subsp. lactis*	*Plesiomonas shigelloides*
Bifidobacterium breve	*Lactobacillus jensenii*	*Prevotella bivia*
Bifidobacterium longum	*Lactobacillus lactis lactis*	*Prevotella corporis*
Branhamella catarrhalis	*Lactobacillus oris*	*Prevotella intermedia*
Brevibacterium linens	*Lactobacillus parabuchneri*	*Propionibacterium acnes*
Campylobacter gracilis	*Lactobacillus vaginalis*	*Proteus mirabilis*
Campylobacter jejuni	*Lactococcus lactis cremoris*	*Proteus vulgaris*
Candida albicans	*Legionella bozemnii*	*Providencia stuartii*
Candida glabrata	*Legionella pneumophila*	*Pseudomonas aeruginosa*
Candida guilliermondi	*Listeria monocytogenes*	*Pseudomonas fluorescens*
Candida krusei	*Micrococcus luteus*	*Pseudomonas putida*
Candida parapsilosis	*Mobiluncus curtisii subsp. curtisii*	*Rahnella aquatilis*
Candida tropicalis	*Mobiluncus curtisii subsp. holmesii*	*Rhizobium radiobacter*
Chlamydophila pneumoniae	*Mobiluncus mulieris*	*Rhodospirillum rubrum*
Chromobacter violaceum	*Moraxella catarrhalis*	*Ruminococcus productus*
Chryseobacterium meningosepticum	*Moraxella lacunata*	*Saccharomyces cerevisiae*
Citrobacter braakii	*Moraxella osloensis*	*Salmonella* Choleraesuis
Citrobacter freundii	*Morganella morganii*	*Salmonella* Minnesota
Clostridium innocuum	*Mycobacterium avium*	*Salmonella* Typhimurium
Clostridium perfringens	*Mycobacterium gordonae*	*Serratia denitrificans*
Clostridium sporogenes	*Mycobacterium smegmatis*	*Serratia marcescens*
Corynebacterium genitalium	*Mycoplasma genitalium*	*Staphylococcus aureus*
Corynebacterium renale	*Mycoplasma hominis*	*Staphylococcus epidermidis*
Corynebacterium xerosis	*Mycoplasma pneumoniae*	*Staphylococcus saprophyticus*
Cryptococcus neoformans	*Neisseria cinerea 832*	*Streptococcus agalactiae*
Cytomegalovirus	*Neisseria cinerea 3306*	*Streptococcus anginosus*
Deinococcus radiodurans	*Neisseria cinerea 3307*	*Streptococcus bovis*
Deinococcus radiopugnans	*Neisseria cinerea 3308*	*Streptococcus dysgalactiae*

Derxia gummosa	*Neisseria cinerea 6317*	*Streptococcus equinis*
Edwardsiella tarda	*Neisseria dentrificans*	*Streptococcus mitis*
Eikenella corrodens	*Neisseria elongata ssp. nitroreducans*	*Streptococcus mutans*
Enterobacter aerogenes	*Neisseria flava*	*Streptococcus pneumoniae*
Enterobacter cloacae	*Neisseria flavescens*	*Streptococcus pyogenes*
Enterococcus avium	*Neisseria kochi*	*Streptococcus salivarius*
Enterococcus faecalis	*Neisseria lactamica*	*Streptococcus sanguis*
Enterococcus faecium	*Neisseria meningitidis 135*	*Streptomyces griseinus*
Epstein Barr Virus	*Neisseria meningitidis Serogroup A*	*Treponema pallidum*
Erwinia herbicola	*Neisseria meningitidis Serogroup B*	*Trichomonas vaginalis*
Erysipelothrix rhusiopathiae	*Neisseria meningitidis Serogroup C*	*Ureaplasma urealyticum*
Escherichia coli	*Neisseria meningitidis Serogroup D*	*Veillonela parvula*
Ewingella americana	*Neisseria meningitidis Serogroup Y*	*Vibrio parahaemolyticus*
Flavobacterium meningosepticum	*Neisseria mucosa*	*Weissella paramesenteroides*
Fusobacterium nucleatum	*Neisseria perflava 837*	*Yersinia enterocolitica*
Gardnerella vaginalis	*Neisseria perflava 911*	
Gemella haemolysans	*Neisseria perflava 6339*	
Gemella morbillorum	*Neisseria perflava 6340*	
Haemophilus ducreyi	*Neisseria perflava 6341*	
Haemophilus influenzae	*Neisseria polysaccharea*	

Table 9: List of Microorganisms Tested Below 1 x 10^6 copies/mL for Analytical Specificity

Microorganism Tested	Concentration Tested in Listed Matrix*	
	Negative Urine Specimen plus cobas® PCR Media	Negative Vaginal Specimen plus cobas® PCR Media
Adenovirus	8x10^5 copies/mL	8x10^5 copies/mL
Chlamydophila pneumoniae	1.1x10^4 copies/mL	1.1x10^4 copies/mL
Gemella morbillorum		4.5 x 10^4 copies/mL
Hepatitis C virus (HCV)	5.6 x 10^4 copies/mL	5.6 x 10^4 copies/mL
Human papillomavirus (HPV) type 16 (SiHa cells)	5x10^4 copies/mL	5x10^4 copies/mL
Human papillomavirus (HPV) type 18 (HeLa cells)	1x10^4 copies/mL	1x10^4 copies/mL
Neisseria cinerea 3308	4x10^5 copies/mL	4x10^5 copies/mL
Prevotella bivia		9x10^4 copies/mL
Prevotella corporis		1.4x10^5 copies/mL
Treponema pallidum	Not Tested	1x10^5 copies/mL
Trichomonas vaginalis		6.5x10^5 copies/mL

*Gray cells indicate concentration tested was ≥ 1 x 106 copies/mL in that matrix

4.5. Interference

Interference testing was performed using **cobas**® PCR Media plus negative urine and negative vaginal swab specimen spiked with CT and NG cultures at ~ 3 x LOD for each target. Eighteen over-the-counter (OTC) products, including contraceptive jelly, lubricants, feminine sprays, anti-fungal cream and anti-itch cream, as well as whole blood, cervical mucus and PBMC cells were tested for interference. Of the 18 OTC products tested, Replens® vaginal moisturizer produced invalid and/or false negative results in the **cobas**® PCR Media plus negative urine panel samples. No interference from Replens® vaginal moisturizer was observed with vaginal swab specimens tested.

The levels of whole blood, mucus and PBMC cells shown in Table 10 represent maximum allowable concentrations which will not interfere with **cobas**® CT/NG Test performance. Concentrations in urine samples were determined using total sample volume, including stabilizing media.

Table 10: Results from Endogenous Interference Testing

	Blood (v/v)		PBMC (cells/mL)		Mucus	
	Conc. Tested	Interference Observed	Conc. Tested	Interference Observed	Conc. Tested	Interference Observed
Urine stabilized in **cobas**® PCR Media	0, 0.25%, 0.35%, 0.5%, 1%, 3%	> 0.35%	0, 1.0E+05, 1.0E+06, 1.0E+07	> 1x 10^5	NT	NT
Vaginal Specimen stabilized in **cobas**® PCR Media	0, 1%, 3%, 5%, 10%	None	0, 1.0E+05, 1.0E+06, 1.0E+07	> 1 x 10^5	Routine level*	None

NT = Not Tested

*Routine level = Quantity of cervical mucus equivalent to amount normally removed prior to sampling

4.6. Precision

Precision of the **cobas**® CT/NG Test was examined in-house using a test panel composed of CT and NG cultures diluted into **cobas**® PCR Media and **cobas**® PCR Media mixed with

negative urine. The precision panel was designed to include members with either CT or NG at approximately the LOD for the panel matrix, members with both CT and NG at approximately the LOD and 2.5 x LOD for the panel matrix and a negative level. Testing was done with three unique lots of **cobas**® CT/NG Test reagents and three instruments for a total of 24 runs. A description of the precision panels and the study performance in % hit rate are shown in Table 11. All positive panel levels yielded the anticipated hit rates. All negative panel levels tested negative throughout the study.

Table 11: In-House Precision Study Hit Rate Analysis

Panel Number	Panel Matrix	Target Conc.		N Tested	N Pos CT	N Pos NG	Hit Rate	95% CI	
		CT	NG					Lower	Upper
1	cobas® PCR Media	Neg	Neg	144	0	0	0%	0.0	2.5
2	cobas® PCR Media	1 X LOD	Neg	144	144	0	100%	97.5	100.0
3	cobas® PCR Media	Neg	1 X LOD	144	0	144	100%	97.5	100.0
4	cobas® PCR Media	1 X LOD	2.5 X LOD	144	144	144	100%	97.5	100.0
5	cobas® PCR Media	2.5 X LOD	1 X LOD	144	144	144	100%	97.5	100.0
1	cobas® PCR Media + Urine	Neg	Neg	144	0	0	0%	0.0	2.5
2	cobas® PCR Media + Urine	1 X LOD	Neg	144	144	0	100%	97.5	100.0
3	cobas® PCR Media + Urine	Neg	1 X LOD	144	0	144	100%	97.5	100.0
4	cobas® PCR Media + Urine	1 X LOD	2.5 X LOD	144	144	144	100%	97.5	100.0
5	cobas® PCR Media + Urine	2.5 X LOD	1 X LOD	144	144	144	100%	97.5	100.0

*99.3 Hit Rate for NG. CT Hit Rate is 100%

5. CLINICAL PERFORMANCE

The clinical performance characteristics of the **cobas**® CT/NG Test were established in two multi-center clinical investigations conducted in the United States. One study evaluated the reproducibility at one internal and two external testing sites. The other study evaluated the sensitivity, specificity, and predictive values of the **cobas**® CT/NG Test on clinical specimens.

5.1. Reproducibility

A Reproducibility Study was performed across lot, testing site, operator, run, and day for the cobas® CT/NG Test using 2 panels prepared from swabs and urine collected in cobas PCR Media. A run for cobas® PCR Media (urine *or* swab) included 3 replicates of each of 5 panel members and 1 positive and 1 negative control (17 total tests). If cobas® PCR Media panels were combined in a run, only 1 positive and 1 negative control were included (32 total tests). The 2 operators at each site performed 2 runs per day, for a total of 3 days of testing per operator per panel type (6 days of testing total for each panel type and reagent lot). Testing was performed with 2 reagent lots (6 days of testing per lot).

Overall, 74 runs were performed, and 72 valid runs were obtained for urine and swab panel types. The 2 invalid runs were due to instrument errors. A total of 1,080 tests were performed on the 5 panel members for each panel type in the valid runs. There was 1 invalid test result in the urine panel type, and 2 invalid test results in the swab panel type. These invalid tests were due to instrument errors.

All valid test results were included in the analyses that reported the percent agreement for CT and NG for each panel type separately. There were no false positive results for either analyte (CT and NG) for both panel types for negative panel members, thus giving negative percent agreement (NPA) of 100% for each analyte.

5.1.1. *C. trachomatis* (Table 12 and Table 13)

Percent agreement for the positive panel members was excellent across both panel types and panel members showing a positive percent agreement (PPA) of 100%.

Analysis of variance components of the Ct values from valid tests performed on positive panel members yielded overall CV (%) ranges from 1.1% to 1.5% for the urine panel type and 1.6% to 1.8% for the swab panel type.

Table 6: *C. trachomatis:* Percent Agreement by Panel Member for Lot, Site/Instrument, and Day — PCR Media/Urine

Panel	Ct	Ct	Percent Agreement *

Member	SD	CV %	Lot			Site/ Instrument			Day		
Negative CT, Negative NG	n/a	n/a	2	100.0	108/108	1	100.0	71/71	1	100.0	72/72
			3	100.0	107/107	2	100.0	72/72	2	100.0	71/71
						3	100.0	72/72	3	100.0	72/72
1x LOD CT, Negative NG	0.54	1.5	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
Negative CT, 1x LOD NG	n/a	n/a	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
1x LOD CT, 2.5x LOD NG	0.48	1.3	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
2.5x LOD CT, 1x LOD NG	0.40	1.1	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72

* For Negative samples, Percent Agreement = (number of negative results/total valid results);
For Positive samples, Percent Agreement = (number of positive results/total valid results)

Table 7: *C. trachomatis:* Percent Agreement by Panel Member for Lot, Site/Instrument, and Day — PCR Media/Swab

Panel Member	Ct SD	Ct CV %	Percent Agreement *								
			Lot			Site/ Instrument			Day		
Negative CT, Negative NG	n/a	n/a	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
1x LOD CT, Negative NG	0.61	1.6	2	100.0	107/107	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	71/71	2	100.0	72/72
						3	100.0	72/72	3	100.0	71/71
Negative CT, 1x LOD NG	n/a	n/a	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	107/107	2	100.0	71/71	2	100.0	71/71
						3	100.0	72/72	3	100.0	72/72
1x LOD CT, 2.5x LOD NG	0.66	1.8	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
2.5x LOD CT, 1x LOD NG	0.59	1.6	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72

* For Negative samples, Percent Agreement = (number of negative results/total valid results);
For Positive samples, Percent Agreement = (number of positive results/total valid results)

5.1.2. *N. gonorrhoeae* (Table 12 and Table 13)

Percent agreement for the positive panel members was excellent across all panel types and panel members. The lowest overall PPA was 99.52% for the "Negative CT, 1 x LOD NG" panel member for PCR Media/Urine panel type.

Analysis of variance components of the Ct values from valid tests performed on positive panel members yielded overall CV (%) ranges from 1.2% to 1.5% for the urine panel type and 1.4% to 1.9% for the swab panel type.

Table 8: *N. gonorrhoeae:* Percent Agreement by Panel Member for Lot, Site/Instrument, and Day — PCR Media/Urine

Panel Member	Ct SD	Ct CV %	Percent Agreement [1]								
			Lot			Site/Instrument			Day		
Negative CT, Negative NG	n/a	n/a	2	100.0	108/108	1	100.0	71/71	1	100.0	72/72
			3	100.0	107/107	2	100.0	72/72	2	100.0	71/71
						3	100.0	72/72	3	100.0	72/72
1x LOD CT, Negative NG	n/a	n/a	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
Negative CT, 1x LOD NG	0.53	1.5	2	99.1	107/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	98.6	71/72
						3	98.6	71/72	3	100.0	72/72
1x LOD CT, 2.5x LOD NG	0.41	1.2	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
2.5x LOD CT, 1x LOD NG	0.54	1.5	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72

[1] For Negative samples, Percent Agreement = (number of negative results/total valid results);
For Positive samples, Percent Agreement = (number of positive results/total valid results)

Table 9: *N. gonorrhoeae:* Percent Agreement by Panel Member for Lot, Site/Instrument, and Day — PCR Media/Swab

Panel Member	Ct SD	Ct CV %	Percent Agreement [1]								
			Lot			Site/ Instrument			Day		
Negative CT, Negative NG	n/a	n/a	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
1x LOD CT, Negative NG	n/a	n/a	2	100.0	107/107	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	71/71	2	100.0	72/72
						3	100.0	72/72	3	100.0	71/71
Negative CT, 1x LOD NG	0.68	1.8	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	107/107	2	100.0	71/71	2	100.0	71/71
						3	100.0	72/72	3	100.0	72/72

Panel Member	Ct SD	Ct CV %	Percent Agreement [1]								
			Lot			Site/ Instrument			Day		
1x LOD CT, 2.5x LOD NG	0.49	1.4	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72
2.5x LOD CT, 1x LOD NG	0.71	1.9	2	100.0	108/108	1	100.0	72/72	1	100.0	72/72
			3	100.0	108/108	2	100.0	72/72	2	100.0	72/72
						3	100.0	72/72	3	100.0	72/72

[1] For Negative samples, Percent Agreement = (number of negative results/total valid results);
For Positive samples, Percent Agreement = (number of positive results/total valid results)

5.2. Clinical Specimen Study

5.2.1. Study Design

Performance characteristics of the **cobas**® CT/NG Test were evaluated in a multi-center clinical study conducted in the United States. Specimens were collected at 12 geographically diverse sites including OB-GYN practices, public and private STD clinics, and family planning centers. A total of 2,851 evaluable male and female, symptomatic and asymptomatic subjects were enrolled. Subjects were classified as symptomatic if the subject reported symptoms indicative of CT or NG infection. Specimens collected from each female subject included urine, a clinician- or self-collected vaginal swab, endocervical swabs, and a cervical sample in PreservCyt® Solution (Hologic Corporation, Bedford MA) obtained with a spatula/cytobrush or a broom. Male subjects provided urethral swabs and urine specimens. Specimens were tested using the **cobas**® CT/NG Test and two commercially available nucleic acid amplification tests (NAAT) for CT and NG. The NAATs were used as reference assays in the clinical study.

For females, urine specimens were collected first. If a cervical cytology test was a scheduled part of the visit, that sample was taken next, followed by a vaginal swab and then endocervical swabs. If a cervical cytology test was not a scheduled part of the visit, a vaginal swab was taken next, followed by endocervical swabs and then the cervical specimen. The order of endocervical swab collection as well as clinician- or self-collection of the vaginal swab was alternated to minimize collection bias. For males, the urethral swabs were collected first in alternating order

and then the urine specimen was collected. All specimens were taken and stored according to the manufacturer's instructions.

5.2.2. Determination of Patient Infected Status

For each subject, a patient infected status (PIS) was determined based on the combined results from the reference assays. A subject was categorized as infected for CT or NG if a minimum of two positive results (at least one from each reference NAAT) was reported, as described in Table 14. Female subjects with positive results on both reference urine specimens and negative results on both reference endocervical swab specimens and the reference cervical sample were categorized as infected for urine and not infected for swab specimens. A subject was classified as non-infected if at least one of the reference NAATs reported negative results for all sample types.

Table 10: Determination of Patient Infected Status

NAAT1 Urine/Endocervical or Urethral Swab	NAAT2 Urine/Endocervical or Urethral Swab	NAAT2 Cervical Specimen in PreservCyt	Patient Infected Status
+/+	+/+	+ or –	Infected
+/+	+/- or -/+	+ or -	Infected
+/- or -/+	+/+	+ or -	Infected
+/-	-/+	+ or -	Infected
-/+	+/-	+ or -	Infected
-/+	-/+	+ or -	Infected
+/-	+/-	+	Infected
+/-	+/-	-	Infected (Urine) Non-Infected (Swabs)
+/- or -/+	-/-	+ or -	Non-Infected
+/+	-/-	+ or -	Non-Infected
-/-	+/+	+ or -	Non-Infected
-/-	+/- or -/+	+ or -	Non-Infected
-/-	-/-	+ or -	Non-Infected

If patient infected status could not be determined due to missing and/or indeterminate results from the reference tests, the subject was excluded from the analysis. PIS could not be determined for one subject.

5.2.3. Study Results

Table 15 through Table 22 summarize the data from the clinical specimen study.

Results from the **cobas**® CT/NG Test were compared with the PIS for calculation of test sensitivity and specificity. A total of 21,988 CT and 21,987 NG results were analyzed by sex, sample type, and the presence of symptoms. The overall sensitivity and specificity for CT was 95.7% and 99.7%. The overall prevalence was 9.0% for CT (6.3% in women and 16.4% in men). The overall sensitivity and specificity for NG was 99.0% and 99.9%. The overall prevalence was 3.6% for NG (1.6% in women, 9.2% in men). Sensitivity, specificity, and prevalence for CT are presented in Table 15. Sensitivity, specificity, and prevalence for NG are presented in Table 16.

A comparison of patient infected status, test results from the reference tests and test results from the **cobas**® CT/NG Test was performed. CT results for female subjects are presented in Table 17, and for male subjects in Table 18. NG results for female subjects are presented in Table 19, and for male subjects in Table 20.

The positive and negative predictive values (PPV and NPV) were calculated using hypothetical prevalence rates and the **cobas**® CT/NG Test sensitivity and specificity determined in the study. The positive and negative predictive value estimates for CT are presented in Table 21, and for NG in Table 22.

Table 11: 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% CI	SPEC	95% CI	PREV (%)	PPV (%)	NPV (%)
Female									
VG	Symp	1073	93.8% (75/80)	(86.2%, 97.3%)	99.7% (990/993)	(99.1%, 99.9%)	7.5	96.2	99.5
	Asymp	1010	94.1% (48/51)	(84.1%, 98.0%)	99.7% (956/959)	(99.1%, 99.9%)	5.0	94.1	99.7

	Overall	2083	93.9% (123/131)	(88.4%, 96.9%)	99.7% (1946/1952)	(99.3%, 99.9%)	6.3	95.3	99.6
Male									
UR	Symp	296	97.3% (72/74)	(90.7%, 99.3%)	99.5% (221/222)	(97.5%, 99.9%)	25.0	98.6	99.1
	Asymp	472	98.1% (51/52)	(89.9%, 99.7%)	99.5% (418/420)	(98.3%, 99.9%)	11.0	96.2	99.8
	Overall	768	97.6% (123/126)	(93.2%, 99.2%)	99.5% (639/642)	(98.6%, 99.8%)	16.4	97.6	99.5
All Combined		2851	95.7% (246/257)	(92.5%, 97.6%)	99.7% (2585/2594)	(99.3%, 99.8%)	9.0	96.5	99.6

[a] VG-S = self-collected vaginal swab; UR = urine.

[b] Symp = symptomatic; Asymp = asymptomatic.

Note: Subjects were designated as being infected with CT if at least 2 NAATs with different target regions gave positive results for the endocervical swab (urethral swab for males) and/or the urine specimen. However, females were categorized as non-infected for any swab specimen if the swab specimens and the PreservCyt specimen (NAAT2) were negative and the urine specimens were positive.

Note: Subjects with designated infection status and valid cobas® CT/NG Test results were considered evaluable and included in this summary table.

Note: CI = (score) confidence interval; PREV = prevalence; SENS = sensitivity; SPEC = specificity; PPV = positive predictive value; NPV = negative predictive value.

Table 12: NG Clinical Performance Compared With Patient Infected Status by Gender, Sample Type, and Symptom Status

Sample Type[a]	Symptom Status[b]	Total (n)	SENS	95% CI	SPEC	95% CI	PREV (%)	PPV (%)	NPV (%)
Female									
VG	Symp	1073	95.7% (22/23)	(79.0%, 99.2%)	99.9% (1049/1050)	(99.5%, 100.0%)	2.1	95.7	99.9
	Asymp	1010	100.0% (10/10)	(72.2%, 100.0%)	100.0% (1000/1000)	(99.6%, 100.0%)	1.0	100.0	100.0
	Overall	2083	97.0% (32/33)	(84.7%, 99.5%)	100.0% (2049/2050)	(99.7%, 100.0%)	1.6	97.0	100.0
Male									
UR	Symp	296	100.0% (64/64)	(94.3%, 100.0%)	99.1% (230/232)	(96.9%, 99.8%)	21.6	97.0	100.0
	Asymp	472	100.0% (7/7)	(64.6%, 100.0%)	100.0% (465/465)	(99.2%, 100.0%)	1.5	100.0	100.0
	Overall	768	100.0% (71/71)	(94.9%, 100.0%)	99.7% (695/697)	(99.0%, 99.9%)	9.2	97.3	100.0
All Combined		2851	99.0% (103/104)	(94.8%, 99.8%)	99.9% (2744/2747)	(99.7%, 100.0%)	3.6	97.2	100.0

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

[a]VG-S = self-collected vaginal swab; UR = urine.

[b] Symp = symptomatic; Asymp = asymptomatic.

Note: Subjects were designated as being infected with NG if at least 2 NAATs with different target regions gave positive results for the endocervical swab (urethral swab for males) and/or the urine specimen.

Note: Subjects with designated infection status and valid cobas® CT/NG Test results were considered evaluable and included in this summary table.

Note: CI = (score) confidence interval; PREV = prevalence; SENS = sensitivity; SPEC = specificity;
PPV = positive predictive value; NPV = negative predictive value.

Table 13: CT Positive/Negative Analysis for Female Patient Infected Status

Patient Infected Status	NAAT1		NAAT2			cobas CT/NG Test	Symptom Status[a]		
	SW	UR	SW	UR	PC Pre	VG	Symp	Asymp	Total
Infected	+	+	+	+	+	+	61	39	100
Infected	+	-	+	-	+	+	2	4	6
Infected	+	-	+	+	+	+	5	0	5
Infected	+	+	+	+	NA	+	2	1	3
Infected	-	+	+	+	+	+	2	1	3
Infected	+	+	+	-	+	+	1	1	2
Infected	+	+	-	+	+	+	1	1	2
Infected	+	+	+	+	+	-	1	0	1
Infected	+	+	+	+	-	+	0	1	1
Infected	+	+	+	-	-	-	0	1	1
Infected	+	+	-	+	-	+	1	0	1
Infected	+	-	+	+	+	-	1	0	1
Infected	+	-	+	-	+	-	1	0	1
Infected	+	-	+	-	-	-	0	1	1
Infected	-	+	+	+	+	-	1	0	1
Infected	-	+	+	+	-	-	1	0	1
Infected	-	+	-	+	NA	-	0	1	1
Total Infected							80	51	131
Non-Infected	-	-	-	-	-	-	957	911	1868
Non-Infected	-	-	-	-	NA	-	16	24	40
Non-Infected	-	-	+	-	-	-	8	3	11
Non-Infected	NA	NA	-	-	-	-	0	9	9
Non-Infected	-	-	+	+	-	-	3	0	3
Non-Infected	-	-	-	-	+	-	0	3	3
Non-Infected	-	-	-	-	-	+	2	1	3
Non-Infected	-	+	-	+	-	-	1	1	2
Non-Infected	-	+	-	-	-	-	0	2	2
Non-Infected	-	-	NA	-	-	-	0	2	2
Non-Infected	-	NA	-	-	-	-	2	0	2
Non-Infected	NA	-	-	-	-	-	2	0	2
Non-Infected	+	-	-	-	-	-	0	1	1
Non-Infected	-	-	+	+	+	+	0	1	1
Non-Infected	-	-	+	-	+	+	0	1	1
Non-Infected	-	-	-	-	+	+	1	0	1
Non-Infected	-	-	-	NA	-	-	1	0	1
Total Non-Infected							993	959	1952

[a] Symp = symptomatic; Asymp = asymptomatic.

Note: Subjects were designated as being infected with CT if at least 2 NAATs with different target regions gave positive results for the endocervical swab and/or urine specimen. However, females were categorized as non-infected for any swab specimen if the swab specimens and the PreservCyt specimen (NAAT2) were negative and the urine specimens were positive.

Note: Subjects with designated infection status and valid **cobas®** CT/NG Test results were considered evaluable and are included in this summary table.

Note: + denotes Positive; - denotes Negative; NA indicates specimen was not obtained for testing or test result was missing/invalid.

Note: SW = endocervical swab; UR = urine; VG = vaginal swab; PC Pre = PreservCyt (pre-aliquot).

Table 14: CT Positive/Negative Analysis for Male Patient Infected Status

Patient Infected Status	NAAT1		NAAT2		cobas CT/NG Test	Symptom Status[a]		
	SW	UR	SW	UR	UR	Symp	Asymp	Total
Infected	+	+	+	+	+	67	43	110
Infected	-	+	-	+	+	3	3	6
Infected	-	+	+	+	+	0	3	3
Infected	+	+	+	-	+	1	1	2
Infected	+	-	+	-	-	0	1	1
Infected	+	-	+	+	+	0	1	1
Infected	-	+	+	-	+	1	0	1
Infected	-	+	-	+	-	1	0	1
Infected	+	+	+	+	-	1	0	1
Total Infected						74	52	126
Non-Infected	-	-	-	-	-	218	412	630
Non-Infected	-	-	+	-	-	1	1	2
Non-Infected	-	-	-	+	-	1	1	2
Non-Infected	-	-	+	+	-	0	2	2
Non-Infected	-	+	-	-	-	0	2	2
Non-Infected	-	-	-	-	+	0	1	1
Non-Infected	-	-	+	+	+	0	1	1
Non-Infected	+	-	-	-	-	1	0	1
Non-Infected	+	+	-	-	+	1	0	1
Total Non-Infected						222	420	642

[a] Symp = symptomatic; Asymp = asymptomatic.

Note: Subjects were designated as being infected with CT if at least 2 NAATs with different target regions gave positive results for the urethral swab and/or the urine specimen.

Note: Subjects with designated infection status and valid **cobas®** CT/NG Test results were considered evaluable and are included in this summary table.

Note: + denotes Positive; - denotes Negative.

Note: SW = urethral swab; UR= urine.

Table 15: NG Positive/Negative Analysis for Female Patient Infected Status

Patient Infected Status	NAAT1		NAAT2			cobas CT/NG Test	Symptom Status[a]		
	SW	UR	SW	UR	PC Pre	VG	Symp	Asymp	Total
Infected	+	+	+	+	+	+	16	9	25
Infected	+	-	+	-	+	+	3	0	3
Infected	-	+	+	+	+	+	1	1	2
Infected	+	+	+	+	+	-	1	0	1
Infected	+	+	+	+	-	+	1	0	1
Infected	+	+	+	-	+	+	1	0	1
Total Infected							23	10	33
Non-Infected	-	-	-	-	-	-	1017	958	1975
Non-Infected	-	-	-	-	NA	-	18	26	44
Non-Infected	NA	NA	-	-	-	-	0	9	9
Non-Infected	+	-	-	-	-	-	4	1	5
Non-Infected	-	-	-	-	+	-	2	2	4
Non-Infected	-	-	NA	-	-	-	2	2	4
Non-Infected	-	-	-	+	-	-	1	1	2
Non-Infected	-	NA	-	-	-	-	2	0	2
Non-Infected	NA	-	-	-	-	-	2	0	2

Patient Infected Status	NAAT1		NAAT2			cobas CT/NG Test	Symptom Status[a]		Total
	SW	UR	SW	UR	PC Pre	VG	Symp	Asymp	
Non-Infected	-	+	-	-	-	-	0	1	1
Non-Infected	-	-	-	-	-	+	1	0	1
Non-Infected	-	-	-	NA	-	-	1	0	1
Total Non-Infected							1050	1000	2050

[a] Symp = symptomatic; Asymp = asymptomatic.
Note: Subjects were designated as being infected with NG if at least 2 NAATs with different target regions gave positive results for the endocervical swab and/or the urine specimen.
Note: Subjects with designated infection status and valid **cobas®** CT/NG Test results were considered evaluable and are included in this summary table.
Note: + denotes Positive; - denotes Negative; NA indicates specimen was not obtained for testing or test result was missing/invalid.
Note: SW = endocervical swab; UR = urine; VG = vaginal swab; PC Pre = PreservCyt (pre-aliquot).

Table 16: NG Positive/Negative Analysis for Male Patient Infected Status

Patient Infected Status	NAAT1		NAAT2		cobas CT/NG Test	Symptom Status[a]		Total
	SW	UR	SW	UR	UR	Symp	Asymp	
Infected	+	+	+	+	+	63	7	70
Infected	+	+	-	+	+	1	0	1
Total Infected						64	7	71
Non-Infected	-	-	-	-	-	227	464	691
Non-Infected	-	-	-	-	+	2	0	2
Non-Infected	-	+	-	-	-	1	1	2
Non-Infected	-	-	+	-	-	1	0	1
Non-Infected	+	-	-	-	-	1	0	1
Total Non-Infected						232	465	697

[a] Symp = symptomatic; Asymp = asymptomatic.
Note: Subjects were designated as being infected with NG if at least 2 NAATs with different target regions gave positive results for the urethral swab and/or the urine specimen.
Note: Subjects with designated infection status and valid **cobas®** CT/NG Test results are considered evaluable and are included in this summary table.
Note: + denotes Positive; - denotes Negative.
Note: SW = urethral swab; UR= urine.

Table 17: Positive Predictive Value and Negative Predictive Value for Hypothetical CT Prevalence

Prevalence (%)	Sensitivity* (%)	Specificity* (%)	PPV (%)	NPV (%)
1	95.7	99.7	73.6	100.0
3	95.7	99.7	89.5	99.9
5	95.7	99.7	93.6	99.8
10	95.7	99.7	96.8	99.5
15	95.7	99.7	98.0	99.2
20	95.7	99.7	98.6	98.9
30	95.7	99.7	99.2	98.2
50	95.7	99.7	99.6	95.9

* Overall sensitivity and specificity were estimated by comparing the **cobas®** CT/NG Test results to patient infected status in both female and male subjects.
Note: PPV = positive predictive value; NPV = negative predictive value.

Table 18: Positive Predictive Value and Negative Predictive Value for Hypothetical NG Prevalence

Prevalence (%)	Sensitivity* (%)	Specificity* (%)	PPV (%)	NPV (%)
1	99.0	99.9	90.2	100.0
3	99.0	99.9	96.6	100.0
5	99.0	99.9	97.9	99.9
10	99.0	99.9	99.0	99.9
15	99.0	99.9	99.4	99.8
20	99.0	99.9	99.6	99.8
30	99.0	99.9	99.7	99.6
50	99.0	99.9	99.9	99.0

*Overall sensitivity and specificity were estimated by comparing the **cobas**® CT/NG Test results to patient infected status in both female and male subjects.
Note: PPV = positive predictive value; NPV = negative predictive value.

5.2.4. Conclusion Drawn from Clinical Specimen Study

In both symptomatic and asymptomatic patients, the **cobas**® CT/NG Test offers high sensitivity, specificity, and positive and negative predictive values for the direct, qualitative detection of CT and NG in male urine specimens and self-collected vaginal swabs. These results are of key importance from both diagnostic and public health perspectives.

6. CONCLUSION

A comparison of the intended use, technological characteristics, and the results of non-clinical analytical and clinical performance studies demonstrate that the **cobas**® CT/NG Test is safe and effective when used in accordance with the product labeling.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Mr. James R. Bonds
Director, Regulatory Affairs
Roche Molecular Systems, Inc.
4300 Hacienda Drive
Pleasanton, CA 94588-0900

JAN 2 4 2012

Re: K110923
Trade Name: cobas® CT/NG Test
Regulation Number: 21 CFR §866.3120
Regulation Name: Chlamydia serological reagents
Regulatory Class: Class I, II
Product Code: MKZ, LSL, OOI
Dated: January 20, 2012
Received: January 23, 2012

Dear Mr. Bonds:

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.

If your device is classified (see above) into class II (Special Controls), it may be subject to such 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 Parts 801 and 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. This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a

legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

cobas® CT/NG Test

Indications for Use Statement

510(k) Number (if known): K110923

Device Name: Roche **cobas®** CT/NG Test

Indications for Use:

Assay

The **cobas®** CT/NG Test is an *in vitro* nucleic acid amplification test that utilizes Polymerase Chain Reaction (PCR) and nucleic acid hybridization for the qualitative detection of *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae (NG)* DNA to aid in the diagnosis of chlamydial and gonococcal disease. The test may be used with vaginal swab specimens self-collected in a clinical setting and male urine from both symptomatic and asymptomatic individuals. Specimens to be tested should be collected in **cobas®** PCR Media.

Ancillary Collection Kits

The **cobas®** PCR Female Swab Sample Kit is used to collect and transport self-collected vaginal swab specimens in a clinical setting. 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 Test. **NOTE: This collection kit should not be used for collection of alternative gynecological specimens.**

The **cobas®** PCR Urine Sample Kit is used to collect and transport male 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 Test. **NOTE: This collection kit should not be used for collection of female urine specimens.**

Prescription Use _X_ (Per 21 CFR Subpart D) OR Over-The-Counter Use (Per 21 CFR Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE — CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) Premarket Submission

510(k) K110923