510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K240197

B Applicant

Roche Molecular Services, Inc.

C Proprietary and Established Names

cobas liat CT/NG/MG nucleic acid test

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QEP	Class II	21 CFR 866.3393 - Device To Detect Nucleic Acids From Non-Viral Microorganism(S) Causing Sexually Transmitted Infections And Associated Resistance Marker(S)	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain market clearance for the cobas liat CT/NG/MG nucleic acid test.

B Measurand:

Chlamydia trachomatis (CT) cryptic plasmid DNA and 23S ribosomal RNA
Neisseria gonorrhoeae (NG) pivNG and NGR9 DNA
Mycoplasma genitalium (MG) mgpC DNA and 23S ribosomal RNA

C Type of Test:

Qualitative, real time nucleic acid amplification test (NAAT)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The cobas liat CT/NG/MG nucleic acid test 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), *Neisseria gonorrhoeae* (NG), and *Mycoplasma genitalium* (MG) nucleic acid in male urine and vaginal swabs, all in cobas PCR Media (Roche Molecular Systems, Inc.).

This test is intended as an aid in the diagnosis of urogenital infections in both symptomatic and asymptomatic individuals

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IVD - For use In Vitro Diagnostic Use Only

D Special Instrument Requirements:

cobas liat System (Analyzer)

IV Device/System Characteristics:

A Device Description:

The cobas liat CT/NG/MG nucleic acid test is performed on the cobas liat analyzer which automates and integrates sample purification, nucleic acid amplification, and detection of the target sequence in biological samples using real-time PCR assays. The assay targets both the Cryptic plasmid and 23S rRNA of CT, the pivNG and NGR9 of NG, and the 23S rRNA and mgpC of MG. An Internal Control (IC) is also included. The IC is present to control for adequate processing of the target bacteria through steps of sample purification, nucleic acid amplification, and to monitor the presence of inhibitors in the PCR processes.

The cobas liat CT/NG/MG nucleic acid test requires the following:

1. A cobas liat CT/NG/MG assay tube which contains the following:
    - Internal process control (IPC)
        - Controls for adequate processing of target bacteria through all steps of assay and to monitor for presence of PCR inhibitors
    - PCR mastermix (assay specific oligonucleotides and polymerase)
    - Co-factor, liat magnetic particles, Lysis buffer, Wash buffer, and Elution buffer
2. Specimen sample stored in cobas PCR Media
3. cobas liat CT/NG/MG Control Kit
    - Contains positive and negative control tubes for use validating new cobas liat CT/NG/MG assay tube lots

4. cobas liat System
5. liat Assay Specific Package (LASP)

B Principle of Operation:

A specimen in cobas PCR Media is collected and then transferred into the assay tube using a transfer pipette. The assay tube is loaded into the analyzer and processing begins. The cobas liat assay tube uses a flexible tube as a sample processing vessel and contains all requisite PCR reagents pre-packed in tube segments that are separated by breakable seals. When a cobas liat assay tube containing a raw biological sample is inserted into the cobas liat analyzer, multiple sample processing actuators in the cobas liat analyzer compress the cobas liat assay tube to selectively release the reagents, moving the sample from one segment to the next, and controlling reaction conditions.

The analyzer automates sample preparation by mixing the sample with an internal control, lysis reagents and liat Magnetic Particles, which are then incubated for nucleic acid binding to the liat Magnetic Particles, and then washed to remove possible inhibitors. Subsequently, the nucleic acid is eluted from the liat Magnetic Particles, mixed with MasterMix and cofactor, and transferred alternately between assay tube segments at different temperatures for rapid PCR amplification and real-time detection.

An embedded microprocessor controls and coordinates these actions to perform all required assay processes with no user intervention required. The detection unit monitors the reaction in real-time while an on-board computer analyzes the collected data and outputs an interpreted result. All assay steps are performed within the closed and self-contained cobas liat assay tube, minimizing cross-contamination between samples. The sample to result time is approximately 20 minutes.

C Instrument Description Information:

1. Instrument Name:

   cobas liat System (Analyzer)

2. Specimen Identification:

   The cobas liat system maintains positive identification of each sample and assay tube during processing and analysis by means of barcode labels.

   Before starting a run, the user is required to scan the assay tube barcode and then scan the sample barcode. The user then transfers the sample into the assay tube and is required to scan the assay tube barcode again before inserting the assay tube into the analyzer and starting the run.

3. Specimen Sampling and Handling:

   Specimen sampling and handling during the assay is controlled automatically using multiple sample processing modules contained within the cobas liat System.

4. Calibration:

   Not applicable.

5. Quality Controls:

   - ***External Control***
     Before using a new lot of cobas liat CT/NG/MG or cobas liat CT/NG assay tubes, the "Lot Validation" procedure must be performed on the analyzer to validate the cobas liat CT/NG/MG or cobas liat CT/NG assay tube lot. The procedure includes running a negative control and a positive control in separate runs. After processing is completed for each control, the system will inform the user that the control result has been accepted. The user can now use that specific lot of assay tubes for processing samples.

   - ***Internal Control***
     An armored RNA is included in the cobas liat CT/NG/MG assay tube. This control acts to monitor the successful execution of the entire assay, from nucleic acid extraction from the targeted microorganisms, amplification, and detection and reporting. The internal control also acts to identify any PCR inhibitors detected in the sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):
cobas 6800/8800 CT/NG
cobas 6800/8800 TV/MG

B Predicate 510(k) Number(s):
K173887
K190433

C Comparison with Predicate(s):

Device & Predicate Device(s):	K240197	K173887	K190433
Device Trade Name	cobas liat CT/NG/MG nucleic acid test; cobas liat CT, NG and MG Control Kit	cobas 6800/8800 CT/NG for use on cobas 6800/8800 Systems	cobas 6800/8800 TV/MG for use on cobas 6800/8800 Systems
General Device Characteristic Similarities and Differences			

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

			preferred specimen type for MG testing in females due to higher sensitivity compared to endocervical swabs and urine. For males, urine is the preferred specimen type due to higher sensitivity compared to meatal swabs. If vaginal swab or male urine is not used and MG testing is negative, further testing with the preferred specimen type may be indicated if M. genitalium infection is strongly suspected.
Analyte targets	Detection of CT, NG, or MG	Detection of CT or NG	Detection of MG or TV
Sample preparation	Automated	Same	Same
Amplification technology	Real-time PCR	Same	Same
Detection chemistry	Assay using different reporter dyes for target and control	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)

VI Standards/Guidance Documents Referenced:

Class II Special Controls as per 21 CFR 866.3393

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A reproducibility study was performed across different sites, lots, days, operators, instruments for panels prepared from vaginal swabs and urine in cobas PCR media. Testing was performed at three external sites with a minimum of three cobas liat analyzers per site. Operators at the CLIA-waived sites that met the definition of intended use operators were considered for this study.

Selected operators were provided with the assay's IFU, Quick Reference Instructions, and the cobas liat system User Guide. Operators were asked to read the materials before beginning any study testing. No instrument training was provided to the operators.

Two operators at each site each tested one panel per specimen type per day (one complete panel consists of three panel members each tested in triplicate) for a total of 15 days. All replicates for each panel member were always tested on the same analyzer. Each panel, per specimen type, consisted of a negative panel member (negative for all three analytes), a low positive panel member, and a moderate positive panel member with each positive panel member being co-formulated with all three analytes.

The Reproducibility Study was executed with a total of 1618 tests consisting of 811 tests for the vaginal specimen type and 807 tests for the urine specimen type. Table 1, Table 2, and Table 3 show the percentage agreement with the expected results by site, lot, day, and run for cobas liat CT/NG/MG by sample type and panel member concentration, respectively for CT, NG, and MG.

Table 1: CT – Agreement with Expected Results by Panel Member for Each Site

Specimen Type	Panel Member Concentration	Percent Agreement with Expected Results (n/N) (95% Confidence Interval)			
		Site 1	Site 2	Site 3	Overall
Vaginal Swab	1-2x LoD	100% (90/90) (95.9% - 100.0%)	100% (89/89) (95.9% – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (269/269) (98.6% - 100.0%)
	3-5x LoD	100% (90/90) (95.9% - 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (270/270) (98.6% - 100.0%)
	Negative	100% (90/90) (95.9% - 100.0%)	100% (83/83) (95.6 – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (263/263) (98.6% - 100.0%)
Male Urine	1-2x LoD	87.8% (79/90) (79.4% - 93.0%)	93.3% (83/89) (86.1% - 96.9%)	91.1% (82/90) (83.4% - 95.4%)	90.7% (244/269) (86.6% - 93.6%)
	3-5x LoD	95.6% (86/90) (89.1% - 98.3%)	98.9% (88/89) (93.9% - 99.8%)	94.4% (85/90) (87.6% - 97.6%)	96.3% (259/269) (93.3% - 98.0%)
	Negative	100% (90/90) (95.9% - 100.0%)	100% (80/80) (95.6% – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% 260/260 (98.5% - 100.0%)

LoD: limit of detection

Table 2: NG – Agreement with Expected Results by Panel Member for Each Site

Specimen Type	Panel Member Concentration	Percent Agreement with Expected Results (n/N) (95% Confidence Interval)			
		Site 1	Site 2	Site 3	Overall
Vaginal Swab	1-2x LoD	100% (90/90) (95.9% - 100.0%)	100% (89/89) (95.9% – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (269/269) (98.6% - 100.0%)
	3-5x LoD	100% (90/90) (95.9% - 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (270/270) (98.6% - 100.0%)
	Negative	100% (90/90) (95.9% - 100.0%)	100% (83/83) (95.6 – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (263/263) (98.6% - 100.0%)
Male Urine	1-2x LoD	100% (90/90) (95.9% - 100.0%)	98.9% (88/89) (93.9% – 99.8%)	100% (90/90) (95.9% - 100.0%)	99.6% (268/269) (97.9% - 99.9%)
	3-5x LoD	100%	100%	100%	100%

		(90/90) (95.9% - 100.0%)	(89/89) (95.9% – 100.0%)	(90/90) (95.9% - 100.0%)	(269/269) (98.6% - 100.0%)
	Negative	100% (90/90) (95.9% - 100.0%)	100% (80/80) (95.6% – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% 260/260 (98.5% - 100.0%)

LoD: limit of detection

Table 3: MG – Agreement with Expected Results by Panel Member for Each Site

Specimen Type	**Panel Member Concentration**	**Percent Agreement with Expected Results (n/N) (95% Confidence Interval)**			
		Site 1	**Site 2**	**Site 3**	**Overall**
Vaginal Swab	1-2x LoD	100% (90/90) (95.9% - 100.0%)	98.9% (88/89) (93.9% – 99.8%)	100% (90/90) (95.9% - 100.0%)	99.6% (268/269) (97.9% - 99.9%)
	3-5x LoD	100% (90/90) (95.9% - 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (270/270) (98.6% - 100.0%)
	Negative	100% (90/90) (95.9% - 100.0%)	100% (83/83) (95.6 – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (263/263) (98.6% - 100.0%)
Male Urine	1-2x LoD	100% (90/90) (95.9% - 100.0%)	100% (89/89) (95.9% – 100.0%)	98.9% (89/90) (94.0% - 100.0%)	99.6% (268/269) (97.9% - 99.9%)
	3-5x LoD	100% (90/90) (95.9% - 100.0%)	100% (89/89) (95.9% – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% (269/269) (98.6% - 100.0%)
	Negative	98.9% (89/90) (94.0% - 100.0%)	100% (80/80) (95.6% – 100.0%)	100% (90/90) (95.9% - 100.0%)	100% 260/260 (98.5% - 100.0%)

LoD: limit of detection

Table 4, Table 5 and Table 6 present the overall percent agreement with the expected results, mean Cycle threshold (Ct) value and between-site, between-lot, between-day, between-run, within-run, and total Ct standard deviation (SD) and percent CV (CV %) for each reproducibility study panel member type run with the cobas liat CT/NG/MG assay, respectively for CT, NG, and MG.

Table 4: Overall Reproducibility Assessment for CT

Sample Type	Panel Member	Percent Agreement (n/N)	Mean Ct	B/t Site SD	B/t Site CV%	B/t Lot SD	B/t Lot CV%	B/t Day SD	B/t Day CV%	B/t Run SD	B/t Run CV%	Within-Run SD	Within-Run CV%	Total SD	Total CV%
Vaginal Swab	1-2xLoD	100% (269/269)	33.4	0.00	0.00	0.53	1.60	0.22	0.67	0.00	0.00	0.84	2.52	1.02	3.06
	3-5x LOD	100% (270/270)	32.1	0.21	0.64	0.58	1.82	0.30	0.93	0.00	0.00	1.00	3.13	1.22	3.79
	Negative	100% (263/263)	…	…	…	…	…	…	…	…	…	…	…	…	…
Urine	1-2xLoD	90.71% (244/269)	34.8	0.15	0.44	0.84	2.41	0.31	0.88	0.00	0.00	0.91	2.61	1.28	3.69
	3-5x LOD	96.28% (259/269)	34.0	0.15	0.45	0.70	2.07	0.23	0.68	0.00	0.00	0.98	2.89	1.24	3.65
	Negative	100% (260/260)	…	…	…	…	…	…	…	…	…	…	…	…	…

B/t: Between

Table 5: Overall Reproducibility Assessment for NG

Sample Type	Panel Member	Percent Agreement (n/N)	Mean Ct	B/t Site SD	B/t Site CV%	B/t Lot SD	B/t Lot CV%	B/t Day SD	B/t Day CV%	B/t Run SD	B/t Run CV%	Within-Run SD	Within-Run CV%	Total SD	Total CV%

Vaginal Swab	1-2xLoD	100% (269/269)	32.2	0.11	0.34	0.59	1.83	0.29	0.89	0.14	0.42	0.59	1.83	0.90	2.79
	3-5x LOD	100% (270/270)	30.9	0.10	0.33	0.15	0.50	0.18	0.57	0.00	0.00	0.41	1.33	0.48	1.56
	Negative	100% (263/263)	…	…	…	…	…	…	…	…	…	…	…	…	…
Urine	1-2xLoD	99.63% (268/269)	32.9	0.16	0.47	0.7	2.12	0.26	0.78	0.46	1.41	0.74	2.25	1.16	3.51
	3-5x LOD	100% (269/269)	31.4	0.07	0.23	0.25	0.80	0.16	0.51	0.00	0.00	0.56	1.79	0.64	2.04
	Negative	100% (260/260)	…	…	…	…	…	…	…	…	…	…	…	…	…

B/t: Between

Table 6: Overall Reproducibility Assessment for MG

Sample Type	Panel Member	Percent Agreement (n/N)	Mean Ct	B/t Site SD	B/t Site CV%	B/t Lot SD	B/t Lot CV%	B/t Day SD	B/t Day CV%	B/t Run SD	B/t Run CV%	Within-Run SD	Within-Run CV%	Total SD	Total CV%
Vaginal Swab	1-2xLoD	99.63% (268/269)	33.3	0.18	0.54	0.52	1.58	0.08	0.23	0.00	0.00	0.89	2.68	1.05	3.16
	3-5x LOD	100% (270/270)	32.0	0.21	0.65	0.66	2.07	0.11	0.34	0.14	0.44	0.88	2.76	1.14	3.55
	Negative	100% (263/263)	…	…	…	…	…	…	…	…	…	…	…	…	…
Urine	1-2xLoD	99.63% (268/269)	34.2	0.23	0.67	0.59	1.73	0.24	0.70	0.00	0.00	1.08	3.16	1.28	3.73
	3-5x LOD	100% (269/269)	33.1	0.27	0.82	0.75	2.25	0.23	0.70	0.10	0.29	1.03	3.11	1.32	4.00
	Negative	99.62% (259/260)	…	…	…	…	…	…	…	…	…	…	…	…	…

B/t: Between

A supplemental reproducibility study was performed at one site across different lots, days, operators and instruments for cobas liat CT/NG/MG nucleic acid test for the detection of CT in urine from urine panels prepared at negative, 1x-2x and 3x-5xLOD concentration levels. There were six total untrained operators and the level of instructional material were the same for this supplemental Reproducibility study. Each operator tested one panel per day for five non-consecutive days for each lot (one complete panel consisted of three panel members). This supplemental Reproducibility Study was executed with a total of 810 evaluable tests on urine panel members. Table 7 demonstrates the percentage agreement with the expected results for each CT panel member, evaluated in vaginal swab or urine clinical matrix, respectively. The average reported Ct value and measurements of variance for CT panel members in vaginal swab and urine clinical matrices are summarized in Table 8. These tables report the following measures of variance: between-instrument, between-lot, between-day, between operator per run, within-run, and total variation.

Table 7: Summary of Within-Laboratory Precision study for CT in Urine Matrix

Panel Member Concentration	Operator	n/N[1]	Agreement with Expected Results (%)
1-2x LoD	1	44/45	97.8%
	2	44/44	100.0%
	3	45/45	100.0%

	4	44/44	100.0 %
	5	45/45	100.0%
	6	45/45	100.0%
3-5x LoD	1	45/45	100.0%
	2	45/45	100.0%
	3	45/45	100.0%
	4	45/45	100.0%
	5	45/45	100.0%
	6	44/44	100.0%
Negative	1	43/44	97.7%
	2	45/45	100.0%
	3	45/45	100.0%
	4	45/45	100.0%
	5	45/45	100.0%
	6	44/44	100.0%

[1]n is the number of tests with expected results. N is the total number of valid tests

Table 8: Overall Precision Assessment for CT

Sample Type	Panel Member	Percent Agreement (n/N)	Mean Ct	Between Instrument		Between Lot		Between Day		Between Operator/Run		Within-Run		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Urine	1-2xLoD	99.63% (267/268)	35.3	0.00	0.00	0.03	0.08	0.00	0.00	0.00	0.00	0.85	2.41	0.85	2.41
	3-5x LOD	100% (269/269)	33.7	0.00	0.00	0.00	0.00	0.00	0.00	0.46	0.35	1.07	3.19	1.17	3.47
	Analyte Negative	99.63% (267/268)	…	…	…	…	…	…	…	…	…	…	…	…	…

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

Cross-reactivity and Microbial Interference
A panel of 181 strains of bacteria, fungi and viruses, including those commonly found in patient specimens, 52 representative strains of non-gonorrhoeae *Neisseria* species and other phylogenetically unrelated organisms, were tested to assess analytical specificity. The organisms listed in Table 9 were spiked at concentrations of ≥1 x 10^6 units/mL* for bacteria or fungi and ≥1 x 10^5 units/mL for viruses into pools of negative vaginal swab specimens collected in cobas PCR Media and negative urine specimens stabilized in cobas PCR Media. Testing was performed with each potential interfering organism in the absence of, as well as mixed with, CT, NG, and MG cultures at ~3x LoD.

Results indicated that 180 of the non-target organisms tested did not generate any false positive or false negative results due to cross-reactivity or interference. One strain of *Neisseria lactamica* (CCUG 26479), at concentrations greater than 1 x 10^4 CFU/mL, interfered with detection of NG at ~3x LoD. At 1 x 10^4 CFU/mL, this *N. lactamica* strain did

not interfere with detection of NG at ~3x LoD, nor did 8 additional strains of *N. lactamica* when tested at concentrations ≥1 x 10^6 CFU/ml.

*Four bacteria could only be tested at a concentration below 1 x 10^6 units/mL and above 7 x 10^4 units/mL due to low stock titers.

Table 9: Microorganisms tested for cobas liat CT/NG/MG nucleic acid test cross-reactivity

Acholeplasma laidlawii	*Eikenella corrodens*	*Micrococcus luteus*	*Pentatrichomonas hominis*
Acholeplasma oculi [a,c]	*Enterobacter aerogenes* (*Klebsiella aerogenes*)	*Mobiluncus curtisii*	*Peptostreptococcus anaerobius*
Acinetobacter calcoaceticus	*Enterobacter cloacae*	*Moraxella catarrhalis*	*Plesiomonas shigelloides*
Acinetobacter Iwoffii	*Enterococcus avium*	*Moraxella lacunata*	*Prevotella bivia*
Actinomyces israelii [a,c]	*Enterococcus faecalis*	*Moraxella osloensis*	*Cutibacterium acnes*
Actinomyces pyogenes (now *Trueperella pyogenes*)	*Enterococcus faecalis* Van B	*Morganella morganii*	*Proteus mirabilis*
Aerococcus viridans	*Enterococcus faecium*	*Mycobacterium smegmatis*	*Proteus vulgaris*
Aeromonas hydrophila	*Enterococcus faecium* Van A	*Mycoplasma faucium* [a,c]	*Providencia stuartii*
Alcaligenes faecalis	*Erwinia herbicola* (now *Pantoea agglomerans*)	*Mycoplasma fermentans*	*Pseudomonas aeruginosa*
Atopobium vaginae *(Fannyhessea vaginae)*	*Erysipelothrix rhusiopathiae*	*Mycoplasma hominis*	*Pseudomonas fluorescens*
Bacillus subtilis	*Escherichia coli*	*Mycoplasma orale*	*Pseudomonas putida*
Bacteroides fragilis	*Flavobacterium meningosepticum* *(Elizabethkingia meningoseptica)*	*Mycoplasma penetrans*	*Rahnella aquatilis*
Bacteroides ureolyticus (*Campylobacter ureolyticus*)	*Fusobacterium nucleatum*	*Mycoplasma pirum*	*Rhizobium radiobacter* *(Agrobacterium tumefaciens)*
Bifidobacterium adolescentis	*Gardnerella vaginalis*	*Mycoplasma pneumoniae*	*Rhodospirillum rubrum*
Bifidobacterium breve	*Gemella haemolysans*	*Mycoplasma primatum*	*Saccharomyces cerevisiae*
Blautia producta	*Giardia Intestinalis*	*Mycoplasma salivarium*	*Salmonella minnesota*
Brevibacterium linens	*Haemophilus ducreyi*	*Mycoplasma spermatophilum*	*Salmonella typhimurium*
Campylobacter jejuni	*Haemophilus influenzae*	*Neisseria cinerea* (4 strains)	*Serratia marcescens*
Candida albicans (2 strains)	Herpes simplex virus I and II	*Neisseria denitrificans* *(Bergeriella denitrifican)*	*Staphylococcus aureus*
Candida glabrata *(Nakaseomyces glabratus)*	HIV-1	*Neisseria elongata* (3 strains)	*Staphylococcus epidermidis*
Candida parapsilosis	Human papilloma virus 16 (CaSki)	*Neisseria flava*	*Staphylococcus saprophyticus*
Candida tropicalis	*Kingella denitrificans*	*Neisseria flavescens* (2 strains)	*Streptococcus agalactiae*
Chlamydia pneumoniae	*Kingella kingae*	*Neisseria lactamica* (9 strains) [b]	*Streptococcus bovis*
Chlamydia psittaci	*Klebsiella oxytoca*	*Neisseria macacae*	*Streptococcus mitis*
Chromobacterium violaceum	*Klebsiella pneumoniae*	*Neisseria meningitidis* Serogroup A	*Streptococcus mutans*
Citrobacter braakii	*Lactobacillus acidophilus*	*Neisseria meningitidis* Serogroup B	*Streptococcus pneumoniae*
Citrobacter freundii	*Lactobacillus brevis* *(Levilactobacillus brevis)*	*Neisseria meningitidis* Serogroup C (4 strains)	*Streptococcus pyogenes*
Clostridium difficile *(Clostridioides difficile)*	*Lactobacillus crispatus*	*Neisseria meningitidis* Serogroup D	*Streptococcus salivarius*
Clostridium perfringens	*Lactobacillus jensenii*	*Neisseria meningitidis* Serogroup W135	*Streptococcus sanguinis*
Corynebacterium genitalium	*Lactobacillus lactis*	*Neisseria meningitidis* Serogroup Y	*Streptomyces griseinus*
Corynebacterium xerosis	*Lactobacillus vaginalis* *(Limosilactobacillus vaginalis)*	*Neisseria mucosa* (3 strains)	*Trichomonas tenax*
Cryptococcus neoformans	*Legionella pneumophila* (2 strains)	*Neisseria perflava*	*Ureaplasma parvum*
Cytomegalovirus	*Leptotrichia buccalis*	*Neisseria polysaccharea*	*Ureaplasma urealyticum* [a,c]
Deinococcus radiodurans	*Leuconostoc mesenteroides*	*Neisseria sicca*	*Veillonella parvula*

		(strain 1 through 3)	
Derxia gummosa	*Leuconostoc paramesenteroides* (*Weissella paramesenteroides*)	*Neisseria subflava* (14 strains)	*Vibrio parahaemolyticus*
Dientamoeba fragilis	*Listeria monocytogenes*	*Paracoccus denitrificans*	*Yersinia enterocolitica*

[a] Organism was tested at a concentration of <1.0e+6 units/mL and >7.0e+4 units/ml.

[b] One strain of organism was tested at a concentration of <1.0e+6 units/mL and >1.0e+4 units/ml.

[c] Tested at highest concentration possible per stock concentration.

Exogenous Substance Interference

The effects of potentially interfering exogenous products that may be present in urine or vaginal swab clinical specimens were evaluated at the concentration listed in Table 10. Testing was executed using pooled analyte negative clinical matrix spiked with potential interferents at clinically relevant concentrations. Interferents were tested in CT/NG/MG negative specimen pools as well as in pools spiked with CT/NG/MG at ~3x LoD for each specimen type, using one lot of reagents. Two culture subtypes were evaluated for each analyte and segregated into two separate multianalyte panels. Five replicates each of CT/NG/MG negative sample and CT/NG/MG positive sample (for each of two culture subtypes per microorganism) were tested with each exogenous substance in each specimen type, except for Azo Urinary Pain Relief, which was tested in urine only.

Of the products tested, no interference was observed in 15 substances when tested at concentrations of 1.5 mg/ml. Azo Urinary Pain Relief and carbomer-containing Replens Long-Lasting Vaginal Moisturizer resulted in false negative results in at least one replicate when tested at higher concentrations. Azo Urinary Pain Relief and Replens Long-Lasting Vaginal Moisturizer at concentrations greater than 0.5 mg/mL and 1.0 mg/mL, respectively, may interfere with the assay performance. Levels of substances tolerated by the assay for all specimen types are shown in Table 10.

Table 10: List of exogenous substances evaluated for interference

Product	Urine (mg/ml)	Vaginal Swab (mg/ml)
Azo Urinary Pain Relief	0.5*	1.5
Clindamycin Phosphate Vaginal Cream	1.5	1.5
Equate Tioconazole 1 Day	1.5	1.5
Equate Vagicaine Anti-Itch Cream	1.5	1.5
7 Day Vaginal Cream	1.5	1.5
K-Y UltraGel	1.5	1.5
Metronidazole Vaginal Cream	1.5	1.5
Monistat Miconazole Nitrate Vaginal Cream	1.5	1.5
Monistat Instant Itch Relief Cream	1.5	1.5
Norforms Deodorant Suppositories	1.5	1.5
Premarin Vaginal Cream	1.5	1.5
Replens Long-Lasting Vaginal Moisturizer	1.0*	1.5
Summer's Even Ultra Freshening Spray	1.5	1.5
VCF- Vaginal Contraceptive Gel	1.5	1.5
Yeast Gard Gel Treatment	1.5	1.5
RepHresh Vaginal Gel	1.5	1.5

*Substances present at concentrations greater than indicated may interfere with cobas liat CT/NG/MG nucleic acid test detection

Endogenous Substance Interference

Endogenous substances that may be present in urine or vaginal swab clinical specimens were evaluated at the concentration listed in Table 13. Testing was executed using pooled clinical specimens spiked with potential endogenous interferents at levels expected in a typical clinical sample. Endogenous substances were tested in CT/NG/MG negative specimen pools as well as in positive specimen pools spiked with CT/NG/MG at ~3x LoD for each relevant specimen type using one lot of reagents. Five replicates each of CT/NG/MG negative sample and CT/NG/MG positive sample (for each of two culture subtypes per microorganism) were tested with each endogenous substance in each relevant sample type. For all endogenous substances tested, no interference was observed. Levels of endogenous substances tolerated by the assay for each specimen types are shown in Table 11.

Table 11: List of endogenous substances evaluated for interference

Endogenous Substance	Conc. in Urine	Conc. in Vaginal Swab
Human cells (PBMC)	$1x10^6$ cells/ml	
Mucus	1 swab dipped into mucus[1]	
Whole blood	10% (v/v)	
Semen	N/A[2]	1.5% (v/v)
Albumin	5% (w/v)	N/A[3]
Bilirubin	1% (w/v)	N/A[3]
Glucose	1% (w/v)	N/A[3]
Acidic pH	pH 4	N/A[3]
Alkaline pH	pH 9	N/A[3]

[1] Mucus swab added to typical volume assessed with the negative sample (~9ml urine, ~4.5ml vaginal swab)

[2] Substance is not applicable to urine specimens

[3] Substance is not applicable to vaginal swab specimen

Competitive Inhibition

To assess competitive inhibition between CT, NG, and MG, at total of six different combinations of low concentration of target (~2x LoD) were mixed with high concentrations of the other targets in both urine and vaginal swab clinical specimen matrices. Each combination was tested in replicates of 10 using one lot of reagents.

Testing results indicated that when one or two target microorganisms were present at high concentrations, no interference was observed for microorganisms that were present at low concentrations (~2x LoD), when tested in both urine and vaginal swab clinical specimen matrices.

4. Assay Reportable Range:

Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Specimen Stability

Two temperature conditions were evaluated for urine and vaginal swab specimen stability. Panel members were prepared by spiking analyte negative urine and vaginal swab matrix with one strain of each analyte, CT (Serovar D), NG (Strain 2948), and MG (Strain M30). All analytes were spiked into either matrix at a final concentration of 3xLoD. Two replicates

of each pooled, unique analyte negative (five) and analyte positive samples (five) were evaluated for a total of 10 replicates. The conditions used for testing are indicated in Table 12 below:

Table 12: Conditions evaluated for specimen stability

Clinical Matrix	Storage Temp	Timepoint	No. of Replicates
Urine	N/A	Baseline/T0 (Immediate)	20 Total
	2-8°C	12 Hours	10 analyte positive 10 analyte negative
		36 Hours	
		60 Hours	
		84 Hours	
	30°C	1 Hour	
		3 Hours	
		5 Hours	
		12 Hours	
		24 Hours	
		36 Hours	
		48 Hours	
Vaginal Swab	N/A	Baseline/T0	20 Total
	2-8°C	24 Hours	10 analyte positive 10 analyte negative
		48 Hours	
		72 Hours	
		96 Hours	
	30°C	24 Hours	
		48 Hours	

The data supported specimen stability claims as reported below:

Urine specimens
Stable for up to two days when stored at 2-8°C.
Stable for 3 hours when stored at 2-30°C.

Vaginal swab specimens
Stable for up to three days when stored at 2-8°C.
Stable for up to one day when stored at 2-30°C.

Reagent Stability

a. *cobas liat CT/NG/MG assay tube*

A real-time stability study is being conducted to determine the shelf-life of the cobas liat CT/NG/MG nucleic acid test. The study is performed with assay tubes stored in the claimed storage condition (2-8°C) and at the upper limit of a room temperature claim (30°C) for short term storage (up to 8 days at 30°C after long-term storage at 2-8°C). The study is being conducted using a negative (NC, cobas liat generic specimen diluent) and the assay external positive control (PCTR, positive for CT, NG, and MG) using three distinct lots of the assay.

Testing has currently been conducted for 10 months and testing will continue for a total of 25 months. The sponsor included the evaluation criteria and the acceptance criteria in the 510(k) submission. Currently, the results of the testing support a shelf life claim for the cobas liat CT/NG/MG assay tube of nine months at 2-8°C.

6. Detection Limit:

The limit of detection of the cobas liat CT/NG/MG nucleic acid test was determined by analyzing a dilution series of two representative strains/serovars of CT (Serovar D and I), NG (Strains 2948 and 891), and MG (Strains M30 and G37). The CT, NG, and MG cultures were diluted in pooled negative urine (UR) or pooled negative vaginal swab (VS) clinical specimens to seven concentration levels. All levels were tested with at least 20 replicates per concentration tested across three unique lots of reagents, over the course of seven non-consecutive days. LoD for each specimen type is shown in Table 13 for CT, NG, and MG, respectively, as the target concentration which can be detected in ≥ 95% of the replicates for all lots.

Table 13: Limit of Detection for CT, NG, and MG in Urine and Vaginal Swabs

Specimen	Strain	CT (EB/mL)	NG (CFU/mL)	MG (cp/mL)
Urine	1	0.085	0.250	0.250
	2	0.784	0.200	0.500
Vaginal Swab	1	0.170	0.500	0.250
	2	0.784	0.200	0.250

Strain 1 combination (CT serovar D, NG Strain 2948, MG Strain M30)
Strain 2 combination (CT serovar I, NG Strain 891, MG Strain G37)

To demonstrate that multi-analyte spike-in (MS) panel members did not impact the detected LoD for each individual analyte, the LoD for single-analyte spike-in (SS) was also evaluated and compared to the LoD determined for multi-analyte spike-in. The LoD between SS and MS samples were assessed for representative subtypes of CT (Serovar I), NG (Strain 2948), and MG (G37). The CT, NG, and MG culture stocks were diluted (either individually or co-formulated) in pooled negative urine clinical specimen matrix. Three dilution levels were prepared for each SS and MS panel members, one above, below and at the hit rate of ≥ 95% as determined in the MS LoD analysis above. Twenty replicates of each concentration were tested using one lot of the cobas liat CT/NG/MG assay tubes, across 20 cobas liat analyzers. The results of this analysis demonstrated that the SS LoD is comparable to the MS LoD (i.e., within a 3-fold difference).

Inclusivity
Inclusivity were performed for an additional 15 CT serovars, 43 NG strains, and 6 MG strains using one lot of reagents. Testing was performed using CT, NG, and MG cultures that were diluted into pools of negative clinical specimens. Three replicates per dilution level were tested for each subtype per specimen type. The lowest level at which all three replicates tested as positive are reported in Table 14, Table 15, and Table 16 for CT, NG, and MG, respectively.

Table 14: CT serovars tested for inclusivity

CT Serovar	Urine	Vaginal Swabs
	Concentration (EB/ml)	
A	0.1	0.2
B	0.4	0.2

Ba	0.4	1
C	0.7	0.7
E	2	36
F	0.4	0.04
G	0.4	0.4
H	0.4	3
J	0.1	0.2
K	0.1	0.04
LGV Type 1	0.1	0.04
LGV Type 2	1600	200
LGV Type 3	0.1	0.7
nvCT	0.1	0.7
Finnish-nvCT	1:100 of Patient Sample	1:100 of Patient Sample

Table 15: NG strains tested for inclusivity

NG Strain	Urine	Vaginal Swabs
	Concentration (CFU/ml)	
27633	0.2	0.5
ATCC 49226	1	0.006
ATCC 700825	0.01	0.001
Clinical Isolate SS169	0.06	0.02
NBL 1606	0.3	0.08
NBL 1952	0.2	0.1
NBL 2012	0.2	0.3
NRL 1977	0.02	0.02
NRL 8042 - Belgium	0.02	0.02
NRL 13477	0.09	0.1
NRL 13819	0.006	0.004
NRL 33155 - Atlanta	0.09	0.001
NRL 33641	0.01	0.07
NRL 35495	0.01	0.07
NRL DAN 09612	0.02	0.03
NRL DN 7896 - DENMARK	0.9	0.3
NRL DN 7901 - DENMARK	0.02	0.02
NRL DOM 362 - Dominican Republic	0.09	0.09
NRL DOM 1271 - Dominican Republic	0.4	0.1
NRL KPO 1148 - KENYA (KPO)	0.2	0.07
NRL KPO 1161 - KENYA (KPO)	0.02	0.02
NRL Peru 33	0.07	0.07
NRL Peru 83	0.02	0.02
NRL PITT 94-4833 - PITTSBURGH (PITT)	0.02	0.02
NRL PITT 94-8561 - PITTSBURGH (PITT)	0.09	0.1
NRL PP 132 - PHILLIPINES	0.09	0.1
NRL SEN 97 P-292 - SENEGAL (SEN)	0.006	0.02
NRL SEN 97 P-301 - SENEGAL (SEN)	0.006	0.07
Roche Diagnostics K.K.,Japan RDN001-00193	0.02	0.03
Roche Diagnostics, Australia 04D125: Darwin Northern Territory, Australia	0.09	0.1
Roche Diagnostics, Australia 04D127: Darwin Northern Territory, Australia	0.09	0.1
Roche Diagnostics, Australia 04D129: Darwin Northern Territory, Australia	0.09	0.1
Roche Diagnostics, Australia 04D130: Darwin Northern Territory, Australia	0.4	0.1
Roche Diagnostics, Australia 04D132: Darwin Northern Territory, Australia	0.09	0.09
Roche Diagnostics, Australia 05D003: Darwin Northern Territory, Australia	0.02	0.03
Roche Diagnostics, Australia 05D004: Darwin Northern Territory, Australia	0.006	0.004
Roche Diagnostics, Australia 4551 - Western Australia	0.02	0.02

Statens Serum Institut 223/06	0.006	0.006
Statens Serum Institut 1498/46	0.02	0.02
Statens Serum Institut 2170/46	0.02	0.02
Statens Serum Institut 2222/46	0.4	0.09
Statens Serum Institut 6973/45	0.09	0.09
UCSF58	0.06	0.07

Table 16: MG strains tested for inclusivity

MG Strain ID	Urine	Vaginal Swabs
	Concentration (copies/ml)	
M2288	2	1
M2300	0.8	0.3
M2341	0.8	1
SEA-1	8	33
M2321	0.8	0.3

7. Assay Cut-Off:

The assay cutoffs for CT, NG, MG, and internal control were initially evaluated using selected clinical study testing data or cultures spiked into clinical matrix (urine stabilized in or vaginal swabs collected in cobas PCR Media). This data (13,651 valid results) was used to confirm adequate separation between the latest Ct value observed in the analyte positive specimens for CT, NG, and MG target detection channels and the assay cut-off. The overall positive and negative agreements for the prospective samples were calculated across specimen types against the matched specimen result from the clinical study comparator assays.

8. Carry-Over:

A carry-over study was conducted for the original cleared cobas Influenza A/B & RSV test for the liat System (K153544) and demonstrated that there was no carry-over or cross contamination observed. The cobas liat CT/NG/MG nucleic acid test for the liat System instrumentation and workflow are identical to the cobas Influenza A/B & RSV for the liat System, therefore additional carry-over studies are not required.

B Comparison Studies:

See Clinical Studies section below.

1. Matrix Comparison:

N/A

C Clinical Studies:

The clinical utility and performance of cobas liat CT/NG/MG nucleic acid test was established in a multi-site, prospective study by comparing the results to a Composite Comparator Algorithm (CCA) or Patient Infected Status (PIS) result derived from a combination of FDA-cleared NAATs for the three analytes. Male urine and vaginal swabs were collected and tested at 13 geographically diverse intended use clinical sites across the US. There were 48 operators that took part in cobas liat

CT/NG/MG testing, of which, 43 represented CLIA-waived operators. Five of the 48 operators represented experienced laboratorians in a moderate complexity laboratory.

Prospectively enrolled female subjects provided four vaginal swab specimens, three for comparator tests and one for the cobas liat CT/NG/MG nucleic acid test. Vaginal swab specimen for the cobas liat CT/NG/MG nucleic acid test was either collected by clinician or self-collected.

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

A total of 4852 subjects (2512 females and 2340 males) were enrolled in the study and provided specimens for collection. Two subjects, declared male at birth, provided vaginal swab specimens.

Upon initial testing, the cobas liat CT/NG/MG nucleic acid test had an invalid rate was 0.6% and, after retesting, had the final invalid rate was 0.1%.

Of the evaluable subjects, the following number of specimens were included in the final clinical performance:

Table 16: Number of specimens included in the clinical performance analysis

Specimen Type	**CT Results**	**NG Results**	**MG Results**
Male Urine	2296	2301	2298
VS CC	1239	1238	1239
VS SC	1234	1234	1233

In addition, a total of 253 archived vaginal and male urine specimens, prospectively collected, were included and tested in this clinical study due to the low NG prevalence observed.

Specimens were tested for CT, NG, and MG using cobas liat CT/NG/MG nucleic acid test and the comparator NAATs. All tests were run according to the respective IFU.

The clinical performance of cobas liat CT/NG/MG nucleic acid test was evaluated by comparing the results from collected specimen types to a PIS or CCA result. Male urine samples were tested with three comparator tests for each analyte (CT, NG, and MG); a concordant result for two out of three comparator tests determined the final PIS status. Vaginal swabs (clinician-collected and self-collected) were tested with three comparator tests for each analyte; a concordant result for two out of three comparator tests determined the CCA result for CT and NG, and the final PIS status for MG. Table 18 below shows the CCA/PIS algorithm for each analyte.

Table 18: Comparator algorithm for CT, NG, and MG

NAAT1	NAAT2	NAAT3	PIS Result	CCA Result
+	+	N/A	Infected	Positive
+	-	+	Infected	Positive
-	+	+	Infected	Positive
-	-	N/A	Not Infected	Negative
+	-	-	Not Infected	Negative
-	+	-	Not Infected	Negative

-	Invalid	+	Indeterminate	Indeterminate
-	Invalid	-	Not Infected	Negative
Invalid	-	+	Indeterminate	Indeterminate
Invalid	-	-	Not Infected	Negative
+	Invalid	-	Indeterminate	Indeterminate
Invalid	+	-	Indeterminate	Indeterminate
+	Invalid	+	Infected	Positive
Invalid	+	+	Infected	Positive
Invalid	Invalid	N/A	Indeterminate	Indeterminate

N/A = Not applicable; NAAT = nucleic acid amplification test

The clinical performance estimates of the cobas liat CT/NG/MG assay nucleic acid test with male urine and vaginal swab (clinician-collected and self-collected vaginal swabs, combined) specimens are shown below for each target pathogen, shown by symptom (symptomatic [Symp] or asymptomatic [Asymp]), in Tables 19 through 21 below. Tabulation of the total number of samples (N) and the number of true positive (TP), false positive (FP), true negative (TN), and false negative (FN) cobas liat CT/NG/MG nucleic acid test results, against the CCA/PIS result, are shown.

Table 19: CT Clinical Performance in Male Urine and Vaginal Swabs against the PIS/CCA result

Specimen Type	Symptom Status	N	TP	FP	TN	FN	Sensitivity		Specificity	
							Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Male Urine	Symp	808	55	1	751	1	98.2% (90.6%, 99.7%)	55/56	99.9% (99.3%, 100.0%)	751/752
	Asymp	1488	53	1	1432	2	96.4% (87.7%, 99.0%)	53/55	99.9% (99.6%, 100.0%)	14332/1433
	Total	2296	108	2	2183	3	97.3% (92.4, 99.1%)	108/111	99.9% (99.7%, 100.0%)	2182/2185
Specimen Type	Symptom Status	N	TP	FP	TN	FN	PPA		NPA	
							Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Vaginal Swabs	Symp	1116	60	3	1052	1	98.4% (91.3%, 99.7%)	60/61	99.7% (99.2%, 99.9%)	1052/1055
	Asymp	1357	47	2	1307	1	97.9% (89.1%, 99.6%)	47/48	99.8% (99.4%, 100.0)	1307/1309
	Total	2473	107	5	2359	2	98.2% (93.6%, 99.5%)	107/109	99.8% (99.5%, 99.9%)	2359/2364

Table 20: NG Clinical Performance in Male Urine and Vaginal Swabs against the PIS/CCA result

Specimen Type	Symptom Status	N	TP	FP	TN	FN	Sensitivity		Specificity	
							Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Prospective Male Urine	Symp	813	68	0	745	0	100.0% (94.7%, 100.0%)	68/68	100.0% (99.5%, 100.0%)	745/745
	Asymp	1488	11	3	1474	0	100.0% (74.1%, 100.0%)	11/11	99.8% (99.4%, 99.9%)	1474/1477
	Total	2301	79	3	2219	0	100.0% (95.4%, 100.0%)	79/79	99.9% (99.6%, 100.0%)	2219/2222
Archived Male Urine	Symp	125	77	0	48	0	100.0% (95.2%, 100.0%)	77/77	100.0% (92.6%, 100.0%)	48/48
	Asymp	38	5	0	33	0	100.0% (56.6%, 100.0%)	5/5	100.0% (89.6%, 100.0%)	33/33
	Total	163	82	0	81	0	100.0% (95.5%, 100.0%)	82/82	100.0% (95.5%, 100.0%)	81/81
Total Male Urine	Symp	938	145	0	793	0	100.0% (97.4%, 100.0%)	145/145	100.0% (99.5%, 100.0%)	793/793
	Asymp	1526	16	3	1507	0	100.0% (80.6%, 100.0%)	16/16	99.8% (99.4%, 99.9%)	1507/1510
	Total	2464	161	3	2300	0	100.0% (97.7, 100.0%)	161/161	99.9% (99.6%, 100.0%)	2300/2303
Specimen Type	Symptom Status	N	TP	FP	TN	FN	PPA		NPA	
							Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Prospective Vaginal Swabs	Symp	1115	22	2	1089	2	91.7% (74.2%, 97.7%)	22/24	99.8% (99.3%, 99.9%)	1089/1091
	Asymp	1357	18	2	1337	0	100.0% (82.4%, 100.0%)	18/18	99.9% (99.5%, 100.0%)	1337/1339
	Total	2472	40	4	2426	2	95.2% (84.2%, 98.7%)	40/42	99.8% (99.6%, 99.9%)	2426/2430
Archived Vaginal Swabs	Symp	42	20	0	22	0	100.0% (83.9%, 100.0%)	20/20	100.0% (83.9%, 100.0%)	22/22
	Asymp	48	25	0	23	0	100.0% (86.7%, 100.0%)	25/25	100.0% (86.7%, 100.0%)	23/23
	Total	90	45	0	45	0	100.0% (92.1%, 100.0)	45/45	100.0% (92.1%, 100.0%)	45/45
Total Vaginal Swabs	Symp	1157	42	2	1111	2	95.5% (84.9%, 98.7%)	42/44	99.8% (99.5%, 100.0%)	1111/1113
	Asymp	1405	43	2	1360	0	100% (91.8%, 100.0%)	43/43	99.9% (99.5%, 100.0%)	1360/1362
	Total	2562	85	4	2471	2	97.7% (92.0%, 99.4%)	85/87	99.8% (99.6%, 99.9%)	2471/2475

Table 21: MG Clinical Performance in Male Urine and Vaginal Swabs against PIS

Specimen Type	Symptom Status	N	TP	FP	TN	FN	Sensitivity		Specificity	
							Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Male Urine	Symp	811	98	9	702	2	98.0% (93.0%, 99.4%)	98/100	98.7% (97.6%, 99.3%)	702/711
	Asymp	1487	104	7	1372	4	96.3% (90.9%, 98.6%)	104/108	99.5% (99.0%, 99.8%)	1372/1379
	Total	2298	202	16	2074	6	97.1% (93.9, 98.7%)	202/208	99.2% (98.8%, 99.5%)	2074/2090
Vaginal Swabs	Symp	1116	120	27	963	6	95.2% (90.0%, 97.8%)	120/126	97.3% (96.1%, 98.1%)	963/990
	Asymp	1356	120	22	1208	6	95.2% (90.0%, 97.8%)	120/126	98.2% (97.3% ,98.8%)	1208/1230
	Total	2472	240	49	2171	12	95.2% (91.9%, 97.3%)	240/252	97.8% (97.1%, 98.3%)	2171/2220

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Positivity of CT, NG, and MG in Male Urine and Vaginal Swabs at Collection Sites:
The positivity rate of the cobas liat CT/NG/MG nucleic acid test for CT, NG, and MG observed during the study is shown for each specimen type, by collection site in Table 22 below.

Table 22: Positivity of CT/NG/MG as Determined by the cobas liat CT/NG/MG nucleic acid test by Specimen Type and Clinical Site

Collection Site	CT		NG		MG	
	Male Urine	VS	Male Urine	VS	Male Urine	VS
1	8.7% (30/343)	9.2% (14/152)	11.0% (38/346)	3.3% (5/152)	14.2% (49/344)	15.1% (23/152)
2	2.6% (9/346)	6.2% (15/241)	1.7% (6/346)	3.7% (9/241)	8.1% (28/346)	14.9% (36/241)
3	11.9% (18/151)	8.2% (30/366)	6.6% (10/151)	0.55% (2/364)	12.6% (19/151)	9.9% (36/365)
4	11.2% (12/107)	0.63% (1/160)	9.3% (10/107)	1.25% (2/160)	18.7% (20/107)	16.3% (26/160)
5	0.0% (0/4)	NC	0.0% (0/4)	NC	25.0% (1/4)	NC
6	0.9% (1/117)	1.2% (1/85)	0.0% (0/118)	1.2% (1/85)	1.7% (2/118)	3.5% (3/85)
7	5.3% (3/57)	5.7% (2/35)	1.8% (1/57)	2.9% (1/35)	14.0% (8/57)	17.1% (6/35)
8	0.0% (0/80)	0.0% (0/19)	2.5% (2/80)	0.0% (0/19)	7.5% (6/80)	10.5% (2/19)
9	1.3% (6/468)	1.9% (10/527)	0.4% (2/469)	2.3% (12/528)	8.8% (41/467)	12.7% (67/527)
10	0.5% (1/198)	1.4% (5/347)	1.0% (2/198)	0.86% (3/347)	4.0% (8/199)	3.2% (11/347)
11	17.1% (18/105)	5.6% (17/305)	4.8% (5/105)	2.0% (6/305)	9.4% (10/106)	15.4% (47/305)
12	3.5% (10/289)	8.8% (12/136)	1.7% (5/289)	1.5% (2/136)	8.0% (23/288)	9.6% (13/136)
13	6.5% (2/31)	5.0% (5/100)	3.2% (1/31)	1.0% (1/100)	9.7% (3/31)	19.0% (19/100)

Note: Two subjects were born male, but were evaluated using self-collected vaginal swabs.
VS: vaginal swabs (clinician-collected vaginal swabs and self-collected)
NC: Non calculable as no female subjects were enrolled at this site

Positive and Negative Predictive Values for Hypothetical Prevalence Rates for Urogenital Samples
The Positive Predictive Value and Negative Predictive Value (PPV and NPV) of the cobas liat CT/NG/MG nucleic acid test were calculated based on the demonstrated sensitivity and specificity (or PPA and NPA estimates for CT and NG in vaginal swabs) in prospectively collected samples tested during the clinical study, using hypothetical prevalence rates. Estimates of the PPV and NPV for the cobas liat CT/NG/MG nucleic acid test are presented for each target organism by specimen type in Tables 23, 24, and 25 below.

Table 23: CT – PPV and NPV for hypothetical CT prevalence

Specimen Type	Hypothetical Prevalence (%)	Sensitivity/ PPA (%)[a]	Specificity/ NPA (%)[a]	PPV (%)	NPV (%)
Male Urine	1	97.3	99.9	91.5	100.0
	3	97.3	99.9	97.0	99.9
	5	97.3	99.9	98.2	99.9
	10	97.3	99.9	99.2	99.7
	15	97.3	99.9	99.5	99.5
	20	97.3	99.9	99.6	99.3
	30	97.3	99.9	99.8	98.9
	50	97.3	99.9	99.9	97.4
Vaginal Swabs	1	98.2	99.8	82.4	100.0
	3	98.2	99.8	93.5	99.9
	5	98.2	99.8	96.1	99.9
	10	98.2	99.8	98.1	99.8
	15	98.2	99.8	98.8	99.7
	20	98.2	99.8	99.1	99.5
	30	98.2	99.8	99.5	99.2
	50	98.2	99.8	99.8	98.2

[a] The sensitivity and specificity (male urine) and PPA and NPA (vaginal swabs) shown were reported for the prospective samples

Table 24: NG – PPV and NPV for hypothetical NG prevalence

Specimen Type	Hypothetical Prevalence (%)	Sensitivity/ PPA (%)[a]	Specificity/ NPA (%)[a]	PPV (%)	NPV (%)
Male Urine	1	100.0	99.9	88.2	100.0
	3	100.0	99.9	95.8	100.0
	5	100.0	99.9	97.5	100.0
	10	100.0	99.9	98.8	100.0
	15	100.0	99.9	99.2	100.0
	20	100.0	99.9	99.5	100.0
	30	100.0	99.9	99.7	100.0
	50	100.0	99.9	99.9	100.0
Vaginal Swabs	1	95.2	99.8	85.4	100.0
	3	95.2	99.8	94.7	99.9
	5	95.2	99.8	96.8	99.7
	10	95.2	99.8	98.5	99.5
	15	95.2	99.8	99.0	99.2
	20	95.2	99.8	99.3	98.8
	30	95.2	99.8	99.6	98.0
	50	95.2	99.8	99.8	95.4

[a] The sensitivity and specificity (male urine) and PPA and NPA (vaginal swabs) shown were reported for the prospective samples

Table 25: MG – PPV and NPV for hypothetical MG prevalence

Specimen Type	Hypothetical Prevalence (%)	Sensitivity (%)[a]	Specificity (%)[a]	PPV (%)	NPV (%)
Male Urine	1	97.1	99.2	56.2	100.0
	3	97.1	99.2	79.7	99.9
	5	97.1	99.2	87.0	99.8
	10	97.1	99.2	93.4	99.7
	15	97.1	99.2	95.7	99.5
	20	97.1	99.2	96.9	99.3
	30	97.1	99.2	98.2	98.8
	50	97.1	99.2	99.2	97.2
Vaginal Swabs	1	95.2	97.8	30.4	100.0
	3	95.2	97.8	57.2	99.8
	5	95.2	97.8	69.4	99.7
	10	95.2	97.8	82.7	99.5
	15	95.2	97.8	88.4	99.1
	20	95.2	97.8	91.5	98.8
	30	95.2	97.8	94.9	98.0
	50	95.2	97.8	97.7	95.4

[a] The sensitivity and specificity shown were reported for the prospective samples

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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