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

I Background Information:

A 510(k) Number

K253759

B Applicant

Roche Molecular Systems, 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 2	866.3393 – Device to detect nucleic acids from non-viral microorganism(s) causing sexually-transmitted infections and associated resistance marker(s)	Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain market clearance for an additional specimen type, female urine.

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/female urine and vaginal swabs, all in cobas PCR Media (Roche Molecular Systems, Inc.).

A vaginal swab (self-collected or clinician-collected) is the preferred specimen type for MG testing in females due to a higher sensitivity when compared to urine. If a female urine is used and MG testing is negative, further testing with a vaginal swab may be indicated if *M. genitalium* infection is suspected.

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

D Special Instrument Requirements:

To be used on the Roche cobas liat system only

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)
   - 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 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 liatMagnetic 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

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 Control:

External Control
Before using a new lot of cobas liat CT/NG/MG assay tubes, the "Lot Validation" procedure must be performed on the analyzer to validate the cobas liat CT/NG/MG 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):
K202408
K190433

C Comparison with Predicate(s):

Device & Predicate Device(s):	K253759	K202408	K190433
Device Trade Name	cobas liat CT/NG/MG	cobas 6800/8800 CT/NG	cobas 6800/8800 TV/MG
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*	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)	cobas 6800/8800 TV/MG for use on 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*

	(MG) nucleic acid in male/female urine and vaginal swabs, all in cobas PCR Media (Roche Molecular Systems, Inc.). A vaginal swab (self-collected or clinician-collected) is the preferred specimen type for MG testing in females due to a higher sensitivity when compared to urine. If a female urine is used and MG testing is negative, further testing with a vaginal swab may be indicated if *M. genitalium* infection is suspected. This test is intended as an aid in the diagnosis of urogenital infections in both symptomatic and asymptomatic individuals.	DNA in male and female urine, clinician-instructed self-collected vaginal swab specimens (collected in a clinical setting), and clinician-collected vaginal swab specimens, endocervical swab specimens, oropharyngeal (throat) swab specimens and anorectal 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.	(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.
Sample Preparation	Automated	Same	Same
Amplification Technology	Real-Time PCR	Same	Same
Specimens Utilized	Male urine Female urine Vaginal swab	Male urine Female urine Self-collected vaginal swab Clinician-collected vaginal swab Endocervical swab Endocervical specimen in PreservCyt Oropharyngeal (throat) swab Anorectal swab specimens	Male urine Female urine Self-collected vaginal swab Clinician-collected vaginal swab Endocervical swab Endocervical specimen in PreservCyt (TV only) Meatal swab (MG only)
Analyte Targets	Detection CT, NG, or MG	Detection CT or NG	Detection MG or TV
Detection Chemistry	Assay using different reporter dyes for targets 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:

   See previous submission, K240197

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

See previous submission, K240197.

4. Detection Limit and Assay Reportable Range:

   See previous submission, K240197

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

   See previous submission, K240197

6. Assay Cut-Off:

   See previous submission, K240197

B Comparison Studies:

1. Method Comparison with Predicate Device:

   See Clinical Studies section below

2. Matrix Comparison:

   Not applicable

C Clinical Studies:

1. Clinical Performance:

   Clinical performance for the cobas liat CT/NG/MG nucleic acid test for vaginal swab and male urine specimens is described in K240197.

   Clinical performance of the cobas liat CT/NG/MG nucleic acid test in female urine specimens was established in a multi-site, prospective study (described in K240197) comparing the results to a Composite Comparator Algorithm (CCA) for CT and NG and Patient Infected Status (PIS) result for MG. CCA for CT and NG was derived from testing female urine specimens on three FDA-cleared NAATs. PIS for MG was derived from testing vaginal specimens on three FDA-cleared NAATs. The subject was considered positive for CT and NG and infected for MG if two out of three comparator NAATs were positive. The subject was considered negative for CT and NG or not infected for MG if two out of three NAATs were negative. Female urine specimens 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. A total of 2512 female subjects were enrolled in the study and provided specimens for collection. Of the evaluable subjects, there were 2459 specimens included in the final clinical performance. Subjects provided a urine specimen that was aliquoted into the respective manufacturers' collection devices and cobas PCR Media.

A supplemental study was conducted to evaluate the performance of cobas liat CT/NG/MG nucleic acid test for the assessment of detecting CT in female urine specimens. Specimen collection was performed at one external site. Nine operators with minimal or no hands-on laboratory training performed the testing. There were a total of 785 prospective samples from subjects who met the study eligibility criteria. Of these 785 samples, there were a total of 751 samples with evaluable results and included in the final data set. The final evaluation was determined by comparing results from cobas liat CT/NG/MG nucleic acid test to CCA.

Analysis of both studies show that the cobas liat CT/NG/MG nucleic acid test detected 8.4% fewer CT infections and 6.9% fewer NG infections in female urine when compared to a vaginal swab CCA versus a female urine CCA. The cobas liat CT/NG/MG nucleic acid test detected 14.1% fewer MG infections in female urine when compared to PIS versus CCA. Clinical performance of the cobas liat CT/NG/MG nucleic acid test is shown in Table 1, 2, 3, and 4.

Table 1: CT Clinical Performance in Female Urine against the CCA Result

Study	Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Supplemental Study	Symptomatic	312	17	2	293	0	100% (81.6%-100%)	99.3% (97.6%-99.8%)
Supplemental Study	Asymptomatic	439	15	3	420	1	93.8% (71.7%-98.9%)	99.3% (97.9%-99.8%)
Supplemental Study	Overall	751	32	5	713	1	97.0% (84.7%-99.5%)	99.3% (98.4%-99.7%)
K240197 Study	Symptomatic	1113	53	2	1054	4	93.0% (83.3%-97.2%)	99.8% (99.3%-99.9%)
K240197 Study	Asymptomatic	1346	40	3	1302	1	97.6% (87.4%-99.6%)	99.8% (99.3%-99.9%)
K240197 Study	Overall	2459	93	5	2356	5	94.9% (88.6%-97.8%)	99.8% (99.5%-99.9%)
Combined	Symptomatic	1425	70	4	1347	4	94.6% (86.9%-97.9%)	99.7% (99.2%-99.9%)
Combined	Asymptomatic	1785	55	6	1722	2	96.5% (88.1%-99.0%)	99.7% (99.2%-99.8%)
Combined	Overall	3210	125	10	3069	6	95.4% (90.4%-97.9%)	99.7% (99.4%-99.8%)

Table 2: NG Clinical Performance in Female Urine against the CCA Result

Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Symptomatic	1111	20	1	1090	0	100% (83.9%-100%)	99.9% (99.5%-100%)
Asymptomatic	1347	17	1	1329	0	100% (81.6%-100%)	99.9% (99.6%-100%)
Overall	2458	37	2	2419	0	100% (90.6%-100%)	99.9% (99.7%-100%)

Table 3: MG Clinical Performance in Female Urine against the CCA Result

Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Symptomatic	1108	101	19	978	10	91.0% (84.2%-95.0%)	98.1% (97.0%-98.8%)
Asymptomatic	1343	98	13	1227	5	95.1% (89.1%-97.9%)	99.0% (98.2%-99.4%)
Overall	2451	199	32	2205	15	93.0% (88.8%-95.7%)	98.6% (98.0%-99.0%)

Table 4: MG Clinical Performance in Female Urine against the PIS Result

Symptom Status	N	TP	FP	TN	FN	Sensitivity (95% CI)	Specificity (95% CI)
Symptomatic	1114	97	23	965	29	77.0% (68.9%-83.5%)	97.7% (96.5%-98.4%)
Asymptomatic	1352	101	12	1215	24	80.8% (73.0%-86.7%)	99.0% (98.3%-99.4%)
Overall	2466	198	35	2180	53	78.9% (73.4%-83.5%)	98.4% (97.8%-98.9%)

2. Clinical Cut-Off

Not applicable

D Expected Values/Reference Range:

Positivity rate for the cobas liat CT/NG/MG nucleic acid test in female urine specimens during the study by collection site is shown below.

Collection Site	CT	NG	MG
1	6.6% (10/151)	2.0% (3/151)	11.3% (17/151)
2	5.4% (13/240)	3.8% (9/240)	11.7% (28/240)
3	7.4% (27/365)	0.6% (2/362)	9.6% (35/363)
4	0.0% (0/161)	1.2% (2/161)	13.0% (21/161)
5	NC	NC	NC
6	2.4% (2/83)	0.0% (0/83)	4.8% (4/83)
7	7.5% (3/40)	2.5% (1/40)	15.0% (6/40)
8	0.0% (0/17)	0.0% (0/17)	0.0% (0/17)
9	1.9% (10/524)	1.5% (8/526)	9.0% (47/523)
10	0.9% (3/348)	0.9% (3/348)	2.9% (10/348)
11	4.6% (14/304)	2.3% (7/304)	11.5% (35/304)

12	9.6% (13/136)	1.5% (2/136)	9.6% (13/136)
13	4.0% (4/101)	2.0% (2/101)	17.0% (17/100)
14 (Supplemental)	4.9% (37/751)	-	-

NC: non calculable as no female subjects were enrolled at this site

E Other Supportive Instrument Performance Characteristics Data:

Not applicable.

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.