January 16th, 2025

Roche Molecular Systems, Inc.
Deborah Leu
Regulatory Affairs Project Manager
4300 Hacienda Drive
Pleasanton, California 94588

Re: K240197
Trade/Device Name: cobas liat CT/NG/MG nucleic acid test
Regulation Number: 21 CFR 866.3393
Regulation Name: Device To Detect Nucleic Acids From Non-Viral Microorganism(S) Causing Sexually Transmitted Infections And Associated Resistance Marker(S)
Regulatory Class: Class II
Product Code: QEP, LSL, MKZ
Dated: January 24, 2024
Received: January 25, 2024

Dear Deborah Leu:

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 (the 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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Himani Bisht -S

Himani Bisht, Ph.D.
Assistant Director
Viral Respiratory and HPV Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K240197

Device Name
cobas liat CT/NG/MG nucleic test

Indications for Use *(Describe)*
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.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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cobas® liat CT/NG/MG nucleic acid test
510(k) Summary

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

Submitter Name	Roche Molecular Systems, Inc.
Address	4300 Hacienda Drive, Pleasanton, CA 94588-2722
Contact	Deborah Leu Phone: 925-523-8362 Email: deborahleu@roche.com
Date Prepared	January 15, 2025
Proprietary Name	**cobas® liat** CT/NG/MG nucleic acid test
Common Name	**cobas® liat** CT/NG/MG
Classification Name	Nucleic Acid Detection System For Non-Viral Microorganism(S) Causing Sexually Transmitted Infections DNA probe, Nucleic Acid Amplification, Chlamydia Neisseria spp. direct serological test reagents
Product Codes	QEP MKZ LSL
Predicate Devices	cobas® 6800/8800 CT/NG, cobas® 6800/8800 TV/MG
Establishment Registration	Roche Molecular Systems, Inc. (2243471)

1. DEVICE DESCRIPTION

The 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 *Chlamydia trachomatis*, the pivNG and NGR9 of *Neisseria gonorrhoeae*, and the 23S rRNA and mgpC of *Mycoplasma genitalium*. 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.

2. 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, 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.

3. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the RMS **cobas® liat** CT/NG/MG nucleic acid test are substantially equivalent to other legally marketed nucleic acid amplification tests intended for the qualitative detection of CT, NG, and MG.

As indicated in Table 1, the RMS **cobas® liat** CT/NG/MG nucleic acid test is substantially equivalent to significant characteristics of the identified predicate device, the currently cleared cobas® 6800/8800 CT/NG (K173887) and cobas® 6800/8800 TV/MG (K190433) for use on cobas® 6800/8800 Systems.

Table 1: Comparison of the cobas® liat CT/NG/MG nucleic acid test and the Predicate Device

	Submitted Device: cobas® liat CT/NG/MG nucleic acid test	Predicate Device: cobas® 6800/8800 CT/NG for use on cobas® 6800/8800 Systems.	Predicate Device: cobas® 6800/8800 TV/MG for use on cobas® 6800/8800 Systems.
Regulation Name	866.3393 866.3120 866.3390	866.3390 866.3120 862.2570	866.3393
Product Code	QEP MKZ LSL	LSL MKZ OOI	QEP

	Submitted Device: cobas® liat CT/NG/MG nucleic acid test	Predicate Device: cobas® 6800/8800 CT/NG for use on cobas® 6800/8800 Systems.	Predicate Device: cobas® 6800/8800 TV/MG for use on cobas® 6800/8800 Systems.
Intended 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.	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), cliniciancollected 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 (selfcollected or cliniciancollected) 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.

	Submitted Device: cobas® liat CT/NG/MG nucleic acid test	Predicate Device: cobas® 6800/8800 CT/NG for use on cobas® 6800/8800 Systems.	Predicate Device: cobas® 6800/8800 TV/MG for use on cobas® 6800/8800 Systems.
Sample Type	Male urine, vaginal swabs	Male and female urine, Self-collected/clinician-collected vaginal swab specimens in cobas® PCR Media, Endocervical swab specimens in cobas® PCR Media, Cervical specimens in PreservCyt® solution.	TV and MG: male and female urine, self-collected vaginal swab specimens (collected in a clinical setting), clinician collected vaginal swab specimens, and endocervical swab specimens, all collected in cobas PCR Media TV only: cervical specimens collected in PreservCyt solution MG only: self-collected meatal swab specimens (collected in a clinical setting) and clinician collected meatal swab specimens
Analyte Targets	Chlamydia trachomatis (CT) Neisseria gonorrhoeae (NG) Mycoplasma genitalium (MG)	Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG)	Trichomonas vaginalis (TV) Mycoplasma genitalium (MG)
Ancillary Collection Kits	cobas® PCR Urine Sample Kit cobas® PCR Media Uni Swab Sample Kit	cobas® PCR Media Dual Swab Sample Kit cobas® PCR Media Uni Swab Sample Kit cobas® PCR Urine Sample Kit	cobas® PCR Media Dual Swab Sample Kit cobas® PCR Media Uni Swab Sample Kit cobas® PCR Urine Sample Kit
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)
Controls Used	Sample processing control (IC) Positive and negative control	Same	Same
Results Analysis	PCR Cycle threshold analysis	Same	Same

4. NON-CLINICAL PERFORMANCE EVALUATION

4.1. Analytical sensitivity (Limit of Detection)

Analytical sensitivity was determined by analyzing a dilution series of two representative strains/serovars of *Chlamydia trachomatis* (CT, Serovar D and I), *Neisseria gonorrhoeae* (NG, Strains 2948 and 891), and *Mycoplasma genitalium* (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 7 concentration levels. All levels were tested with at least 20 replicates per concentration tested across 3 unique lots of reagents. LoD for each specimen type is shown in Table 2, Table 3, and Table 4 for CT, NG, and MG, respectively as the target concentration which can be detected in ≥ 95% of the replicates for all lots.

Table 2: CT concentration levels with at least 95% observed hit rate for all lots tested

Specimen Types	CT Serovar D LoD (EB/mL)	CT Serovar D Mean Ct Value	CT Serovar I LoD (EB/mL)	CT Serovar I Mean Ct Value
Urine in cobas® PCR Media	0.085	36.2	0.784	36.0
Vaginal Swab in cobas® PCR Media	0.170	35.3	0.784	35.7

EB = Elementary Bodies

Table 3: NG concentration levels with at least 95% observed hit rate for all lots tested

Specimen Types	NG Strain 2948 LoD (CFU/mL)	NG Strain 2948 Mean Ct Value	NG Strain 891 LoD (CFU/mL)	NG Strain 891 Mean Ct Value
Urine in cobas® PCR Media	0.250	34.7	0.200	34.5
Vaginal Swab in cobas® PCR Media	0.500	34.2	0.200	34.5

CFU = Colony Forming Units

Table 4: MG concentration levels with at least 95% observed hit rate for all lots tested

Specimen Types	MG M30 LoD (cp/mL)	MG M30 Mean Ct Value	MG G37 LoD (cp/mL)	MG G37 Mean Ct Value
Urine in cobas® PCR Media	0.250	35.2	0.500	33.7

Specimen Types	MG M30 LoD (cp/mL)	MG M30 Mean Ct Value	MG G37 LoD (cp/mL)	MG G37 Mean Ct Value
Vaginal Swab in cobas® PCR Media	0.250	34.4	0.250	33.9

cp = copies

4.2. Inclusivity

Inclusivity was 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 spiked 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 5, Table 6, and Table 7 for CT, NG, and MG, respectively.

Table 5: Inclusivity testing for CT serovars

Serovar Type or Variant	Urine Specimens (EB/mL)	Vaginal Swab Specimens (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 6: Inclusivity testing for NG strains

Strain ID	Urine Specimens (CFU/mL)	Vaginal Swab Specimens (CFU/mL)
ATCC 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

Strain ID	Urine Specimens (CFU/mL)	Vaginal Swab Specimens (CFU/mL)
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 7: Inclusivity testing for MG strains

Strain ID	MG (copies/mL)	
	Urine Specimens	Vaginal Swab Specimens
M2288	2	1
M2300	0.8	0.3
M2341	0.8	1
SEA-1	8	33
M2321	0.8	0.3
TW 10-5G	0.08	0.08

4.3. Analytical specificity/cross reactivity

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 8 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 8: Microorganisms tested for analytical specificity/cross reactivity

Acholeplasma laidlawii	*Eikenella corrodens*	*Mobiluncus curtisii*	*Peptostreptococcus anaerobius*
Acholeplasma oculi [a,c]	*Enterobacter aerogenes* (*Klebsiella aerogenes*)	*Moraxella catarrhalis*	*Plesiomonas shigelloides*
Acinetobacter calcoaceticus	*Enterobacter cloacae*	*Moraxella lacunata*	*Prevotella bivia*
Acinetobacter lwoffii	*Enterococcus avium*	*Moraxella osloensis*	*Cutibacterium acnes*
Actinomyces israelii [a,c]	*Enterococcus faecalis* (2 strains)	*Morganella morganii*	*Proteus mirabilis*
Actinomyces pyogenes (*Trueperella pyogenes*)	*Enterococcus faecium* (2 strains)	*Mycobacterium smegmatis*	*Proteus vulgaris*
Aerococcus viridans	*Erwinia herbicola* (*Pantoea agglomerans*)	*Mycoplasma faucium* [a,c]	*Providencia stuartii*
Aeromonas hydrophila	*Erysipelothrix rhusiopathiae*	*Mycoplasma fermentans*	*Pseudomonas aeruginosa*
Alcaligenes faecalis	*Escherichia coli*	*Mycoplasma hominis*	*Pseudomonas fluorescens*
Atopobium vaginae (*Fannyhessea vaginae)*	*Flavobacterium meningosepticum (Elizabethkingia meningoseptica)*	*Mycoplasma orale*	*Pseudomonas putida*
Bacillus subtilis	*Fusobacterium nucleatum*	*Mycoplasma penetrans*	*Rahnella aquatilis*
Bacteroides fragilis	*Gardnerella vaginalis*	*Mycoplasma pirum*	*Rhizobium radiobacter* (*Agrobacterium tumefaciens)*
Bacteroides ureolyticus (*Campylobacter ureolyticus*)	*Gemella haemolysans*	*Mycoplasma pneumoniae*	*Rhodospirillum rubrum*
Bifidobacterium adolescentis	*Giardia Intestinalis*	*Mycoplasma primatum*	*Saccharomyces cerevisiae*

Bifidobacterium breve	*Haemophilus ducreyi*	*Mycoplasma salivarium*	*Salmonella minnesota*
Blautia producta	*Haemophilus influenzae*	*Mycoplasma spermatophilum*	*Salmonella typhimurium*
Brevibacterium linens	Herpes simplex virus I	*Neisseria cinerea* (4 strains)	*Serratia marcescens*
Campylobacter jejuni	Herpes simplex virus II	*Neisseria denitrificans (Bergeriella denitrifican)*	*Staphylococcus aureus*
Candida albicans (2 strains)	HIV-1	*Neisseria elongata* (3 strains)	*Staphylococcus epidermidis*
Candida glabrata (*Nakaseomyces glabratus)*	Human papilloma virus 16 (CaSki cells)	*Neisseria flava*	*Staphylococcus saprophyticus*
Candida parapsilosis	*Kingella denitrificans*	*Neisseria flavescens* (2 strains)	*Streptococcus agalactiae*
Candida tropicalis	*Kingella kingae*	*Neisseria lactamica* (9 strains)[b]	*Streptococcus bovis*
Chlamydia pneumoniae	*Klebsiella oxytoca*	*Neisseria macacae*	*Streptococcus mitis*
Chlamydia psittaci	*Klebsiella pneumoniae*	*Neisseria meningitidis* Serogroup A	*Streptococcus mutans*
Chromobacterium violaceum	*Lactobacillus acidophilus*	*Neisseria meningitidis* Serogroup B	*Streptococcus pneumoniae*
Citrobacter braakii	*Lactobacillus brevis (Levilactobacillus brevis)*	*Neisseria meningitidis* Serogroup C (4 strains)	*Streptococcus pyogenes*
Citrobacter freundii	*Lactobacillus crispatus*	*Neisseria meningitidis* Serogroup D	*Streptococcus salivarius*
Clostridium difficile (*Clostridioides difficile)*	*Lactobacillus jensenii*	*Neisseria meningitidis* Serogroup W135	*Streptococcus sanguinis*
Clostridium perfringens	*Lactobacillus lactis*	*Neisseria meningitidis* Serogroup Y	*Streptomyces griseinus*
Corynebacterium genitalium	*Lactobacillus vaginalis* (*Limosilactobacillus vaginalis)*	*Neisseria mucosa* (3 strains)	*Trichomonas tenax*
Corynebacterium xerosis	*Legionella pneumophila* (2 strains)	*Neisseria perflava*	*Ureaplasma parvum*
Cryptococcus neoformans	*Leptotrichia buccalis*	*Neisseria polysaccharea*	*Ureaplasma urealyticum* [a,c]
Cytomegalovirus	*Leuconostoc mesenteroides*	*Neisseria sicca* (3 strains)	*Veillonella parvula*
Deinococcus radiodurans	*Leuconostoc paramesenteroides* (*Weissella paramesenteroides*)	*Neisseria subflava* (14 strains)	*Vibrio parahaemolyticus*
Derxia gummosa	*Listeria monocytogenes*	*Paracoccus denitrificans*	*Yersinia enterocolitica*
Dientamoeba fragilis	*Micrococcus luteus*	*Pentatrichomonas hominis*	-

[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.

4.4. Interference

The effects of over-the-counter or prescription products that may be present in urine or vaginal swab clinical specimens were evaluated at the concentration listed in Table 9. Testing was executed using pooled clinical specimens spiked with potential interferents at levels expected from normal patient usage. Interferents 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 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 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 9.

Table 9: List of products tested for interference

Product Name	Urine (mg/mL)	Vaginal Swabs (mg/mL)
Azo Urinary Pain Relief (urine only)	0.5*	-
Clindamycin Phosphate Vaginal Cream	1.5	1.5
Equate tioconazole 1 Day	1.5	1.5
Equate Vagicaine Anti-Inch Cream	1.5	1.5
Estradiol Vaginal Cream	1.5	1.5
7 Day vaginal cream	1.5	1.5
K-Y® UltraGel	1.5	1.5
Metronidazole Vaginal Gel	1.5	1.5
Monistat Miconazole Nitrate Vaginal Cream (2%)	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

Product Name	Urine (mg/mL)	Vaginal Swabs (mg/mL)
Replens™ Long-Lasting Vaginal Moisturizer	1.0*	1.5
Summer's Eve 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

*Note: Concentrations above this level may cause interference in clinical samples.

Endogenous substances 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 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 10

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

Endogenous Substance	Urine	Vaginal Swab
Human cells (PBMCs) cells/mL	1.0E+06	1.0E+06
Mucus	1 swab dipped into mucus	1 swab dipped into mucus
Whole blood (v/v)	10%	10%
Semen (v/v) (vaginal swab only)	-	1.5%
Albumin (w/v) (urine only)	5%	-
Bilirubin (w/v) (urine only)	1% (w/v)	-
Glucose (w/v) (urine only)	1% (w/v)	-
Acidic pH (urine only)	pH 4	-
Alkaline pH (urine only)	pH 9	-

4.5. 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.

5. REPRODUCIBILITY STUDIES

A reproducibility study was performed across different sites, lots, days, operators, instruments for **cobas® liat** CT/NG/MG panels prepared from vaginal swabs and urine in **cobas®** PCR media. Testing was performed at three external sites with a minimum of 3 **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 assay or instrument training was provided to the operators.

Two operators at each site each tested 1 panel per specimen type per day (1 complete panel consists of 3 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 3 analytes), a low positive panel member, and a moderate positive panel member with each positive panel member being co-formulated with all 3 analytes. For each panel member, approximately 270 results were produced.

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 11, Table 12 and Table 13 show the site-to-site Reproducibility Study results for **cobas® liat** CT/NG/MG by sample type and panel member concentration, respectively, for CT, NG, and MG.

Table 11: Summary CT of site-to-site reproducibility results with cobas® liat CT/NG/MG

Specimen Type	Panel Member Concentration	Site 1*	Site 2*	Site 3*	Overall*
Vaginal	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%)
Vaginal	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%)
Vaginal	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%)
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%)
Urine	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%)
Urine	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%)

Note: LoD: limit of detection

*Percent Agreement with expected results (n/N) (95% Confidence Interval)

Table 12: Summary NG of site-to-site reproducibility results with cobas® liat CT/NG/MG

Specimen Type	Panel Member Conc.	Site 1*	Site 2*	Site 3*	Overall*
Vaginal	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%)
Vaginal	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%)
Vaginal	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%)
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%)
Urine	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%)
Urine	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%)

Note: LoD: limit of detection.

*Percent Agreement with expected results (n/N) (95% Confidence Interval)

Table 13: Summary MG of site-to-site reproducibility results with cobas® liat CT/NG/MG

Specimen Type	Panel Member Conc.	Site 1*	Site 2*	Site 3*	Overall*
Vaginal	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%)
Vaginal	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%)
Vaginal	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%)
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%)

Specimen Type	Panel Member Conc.	Site 1*	Site 2*	Site 3*	Overall*
Urine	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%)
Urine	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%)

Note: LoD : limit of detection.

*Percent Agreement with expected results (n/N) (95% Confidence Interval)

Table 14, Table 15 and Table 16 present the total SD, and total percent CV (%) for Cycle Threshold Values from the Reproducibility Study for each specimen panel type run in **cobas® liat** CT/NG/MG, respectively, for CT, NG, and MG.

Table 14: CT - Overall mean estimate, standard deviations, and coefficients of variation (%) for cycle threshold values by sample type and expected concentration for cobas® liat CT/NG/MG by sample type and positive panel member concentration

Sample Type	Panel Member Concen-tration	n/N[a]	Mean Ct	Bet-ween Site SD	Be-tween Site CV%	Be-tween Lot SD	Be-tween Lot CV%	Be-tween Day SD	Be-tween Day CV%	Between Operator / Run SD	Between Operator/ Run CV%	Within Run SD	Within RunCV %	Total SD	Total CV%
Vaginal	1×-2× LoD	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
Vaginal	3×-5× LoD	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
Urine	1×-2× LoD	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
Urine	3×-5× LoD	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

Ct: cycle threshold; CV%: percent coefficient of variation; LOD: Limit of Detection; SD: standard deviation.

[a]n is the number of tests in agreement with expected results. N is the total number of valid tests for the panel member.

Table 15: NG - Overall mean estimate, standard deviations, and coefficients of variation (%) for cycle threshold values by sample type and expected concentration for cobas® liat CT/NG/MG by sample type and positive panel member concentration

Sample Type	Panel Member Concen-tration	n/N[a]	Bet-ween Site SD	Be-tween Site CV%	Be-tween Lot SD	Be-tween Lot CV%	Be-tween Day SD	Be-tween Day CV%	Between Operator / Run SD	Between Operator / Run CV%	Within Run SD	Within RunCV %	Total SD	Total CV%	Total CV%
Vaginal	1×-2× LoD	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
Vaginal	3×-5× LoD	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
Urine	1×-2× LoD	268/269	32.9	0.16	0.47	0.70	2.12	0.26	0.78	0.46	1.41	0.74	2.25	1.16	3.51
Urine	3×-5× LoD	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

Ct: cycle threshold; CV%: percent coefficient of variation; LOD: Limit of Detection; SD: standard deviation.

[a]n is the number of tests in agreement with expected results. N is the total number of valid tests for the panel member.

Table 16: MG - Overall mean estimate, standard deviations, and coefficients of variation (%) for cycle threshold values by sample type and expected concentration for cobas® liat CT/NG/MG by sample type and positive panel member concentration

Sample Type	Panel Member Concentration	n/N[a]	Bet-ween Site SD	Be-tween Site CV%	Be-tween Lot SD	Be-tween Lot CV%	Be-tween Day SD	Be-tween Day CV%	Between Operator/ Run SD	Between Operator / Run CV%	Within Run SD	Within RunCV %	Total SD	Total CV %	Total CV %
Vaginal	1×-2× LoD	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
Vaginal	3×-5× LoD	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
Urine	1×-2× LoD	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
Urine	3×-5× LoD	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

Ct: cycle threshold; CV%: percent coefficient of variation; LOD: Limit of Detection; SD: standard deviation.

[a]n is the number of tests in agreement with expected results. N is the total number of valid tests for the panel member.

In the Reproducibility Study, the PPA for CT in urine panel members was less than the expected 95%. Therefore, a supplemental Precision Study was performed at one site across different lots, days, operators and instruments for **cobas® liat** CT/NG/MG 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 Precision Study. Each operator tested 1 panel per day for 5 non-consecutive days for each lot (1 complete panel consisted of 3 panel members). This supplemental Precision Study was executed with a total of 810 evaluable tests on urine panel members.

Table 17 shows the supplemental between operator Precision Study for **cobas® liat** CT/NG/MG by panel member concentration for CT in urine.

Table 17: Summary of CT Precision/Repeatability study results

Panel Member Concentration	Operator	n/N [a]	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%

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

Table 18 shows the supplemental precision Study for **cobas® liat** CT/NG/MG standard deviation (SD) and coefficient of variation (CV) of Cycle Threshold Values for each factor as well as the total SD and total CV (%) for each positive panel member.

Table 18: CT - Overall mean estimate, standard deviations, and coefficients of variation (%) for cycle threshold values and expected concentration for cobas® liat CT/NG/MG by positive panel member concentration in urine

Panel Member Concentration	n/N[a]	Mean Ct	Between Instrument SD	Between Instrument CV%	Between Lot	Be-tween Lot CV%	Be-twee n Day SD	Be-tween Day CV%	Between Operator/ Run SD	Between Operato r/Run CV%	With in Run SD	Within Run CV%	Total SD	Total CV%
1x-2x LoD	267/2 68	35.3	0.00	0.00	0.03	0.08	0.0 0	0.00	0.00	0.00	0.8 5	2.41	0.8 5	2.4 1
3x-5x LoD	269/2 69	33.7	0.00	0.00	0.00	0.00	0.0 0	0.00	0.46	1.35	1.0 7	3.19	1.1 7	3.4 7

Note: Ct = cycle threshold, CT=*Chlamydia trachomatis*, CV(%) = percent coefficient of variation, LOD = Limit of Detection, MG=*Mycoplasma genitalium*, NG=*Neisseria gonorrhoeae*, SD = standard deviation.

[a]n is the number of tests in agreement with expected results. N is the total number of valid tests for the panel member.

6. CLINICAL PERFORMANCE EVALUATION

6.1. Clinical study

The clinical utility and performance of **cobas® liat** CT/NG/MG was established in a multi-site, prospective study by comparing the results to a Patient Infected Status (PIS) or a Composite Comparator Algorithm (CCA) derived from a combination of FDA-cleared NAATs for the 3 analytes. A CCA result was generated for vaginal swabs tested for CT or NG. A PIS result was generated for the remaining specimen types and analyte (i.e., MG in vaginal swabs and CT/NG/MG in male urine). 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.

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

specimens. Of these subjects, 72 were non-evaluable due to protocol deviations and incidents (18), invalid cobas and/or final comparator result (45), or sample collection incidents (9). Of the evaluable subjects, 2304 male subjects provided 2302 male urine specimens (2 subjects provided vaginal swab specimens) and 2476 females provided 1240 clinician-collected vaginal swabs and 1236 self-collected vaginal swabs for evaluation in the clinical study.

Prospectively enrolled female subjects provided 4 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.

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

The clinical performance of **cobas® liat** CT/NG/MG was evaluated by comparing the results from collected specimen types to a pre-specified PIS/CCA result. The PIS/CCA result for each analyte was derived from a combination of 3 comparator NAATs (NAAT1, NAAT2, and NAAT3). If NAAT1 and NAAT2 are concordant, then the final PIS/CCA result for the respective analyte is the concordant result obtained from NAAT1 and NAAT2. If NAAT1 and NAAT2 are discordant, then NAAT3 is performed to be the tiebreaker between the first 2 discordant results. Table 19 below shows the PIS and CCA algorithm for each analyte.

Table 19: Determination of the PIS/CCA result for CT, NG, and MG, respectively

NAAT 1	NAAT 2	NAAT 3 (if needed)	Patient Infected Status[a]	Composite Comparator Algorithm
+	+	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

NAAT 1	NAAT 2	NAAT 3 (if needed)	Patient Infected Status[a]	Composite Comparator Algorithm
+	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.

[a] The results from NAAT1 and NAAT2 determined if NAAT3 needed to be performed. The "Infected" or "Not Infected" patient infected status was derived from the total combination of results obtained from the reference NAATs.

The sample types of male urine and vaginal swab were used to create the PIS and CCA results, respectively, for men and women. The **cobas® liat** CT/NG/MG results of each analyte from each

sample type (male urine and vaginal swab) were compared to the PIS/CCA result to determine the clinical performance of the assay. Sensitivity (SENS), specificity (SPEC), positive percent agreement (PPA), and negative percent agreement (NPA) of **cobas® liat** CT/NG/MG were calculated separately for CT, NG, and MG.

Supplementation with archived specimens was included in this study due to the expected low NG prevalence for male urine and vaginal swabs. The archived specimens were prospectively collected samples from a prior clinical trial study (K173887).

6.2. Performance results

Sensitivity/PPA and specificity/NPA of **cobas® liat** CT/NG/MG as defined by the PIS/CCA results are presented by sample type, and symptom status in Table 20 for CT, Table 21 for NG collected specimens, and Table 22 for MG.

Upon initial testing, the **cobas® liat** CT/NG/MG invalid rate was 0.6% and after retesting the final invalid rate was 0.1%.

Table 20: CT - clinical performance of cobas® liat CT/NG/MG compared with PIS/CCA by specimen type and symptom status

Specimen Type	Symptom Status	N	Sensitivity Estimate (95% CI)	Sensitivity n/N	Specificity Estimate (95% CI)	Specificity n/N
Male Urine	Symptomatic	808	98.2% (90.6%, 99.7%)	55/56	99.9% (99.3%, 100.0%)	751/752

	Asymptomatic	1488	96.4% (87.7%, 99.0%)	53/55	99.9% (99.6%, 100.0%)	1432/1433
	Total	2296	97.3% (92.4%, 99.1%)	108/111	99.9% (99.7%, 100.0%)	2183/2185
Specimen Type	Symptom Status	N	Positive Percent Agreement	Positive Percent Agreement	Negative Percent Agreement	Negative Percent Agreement
			Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Vaginal Swabs	Symptomatic	1116	98.4% (91.3%, 99.7%)	60/61	99.7% (99.2%, 99.9%)	1052/1055
	Asymptomatic	1357	97.9% (89.1%, 99.6%)	47/48	99.8% (99.4%,100.0%)	1307/1309
	Total	2473	98.2% (93.6%, 99.5%)	107/109	99.8% (99.5%, 99.9%)	2359/2364

CI: confidence interval

Table 21: NG - Clinical performance of cobas® liat CT/NG/MG compared with PIS/CCA by specimen type and symptom status

Specimen Type	Symptom Status	N	Sensitivity	Sensitivity	Specificity	Specificity
			Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Male Urine	Symptomatic	813	100.0% (94.7%, 100.0%)	68/68	100.0% (99.5%, 100.0%)	745/745
	Asymptomatic	1488	100.0% (74.1%, 100.0%)	11/11	99.8% (99.4%, 99.9%)	1474/1477
	Total	2301	100.0% (95.4%, 100.0%)	79/79	99.9% (99.6%, 100.0%)	2219/2222
Archived Male Urine	Symptomatic	125	100.0% (95.2%, 100.0%)	77/77	100.0% (92.6%, 100.0%)	48/48
	Asymptomatic	38	100.0% (56.6%, 100.0%)	5/5	100.0% (89.6%, 100.0%)	33/33
	Total	163	100.0% (95.5%, 100.0%)	82/82	100.0% (95.5%, 100.0%)	81/81
Overall Male Urine	Symptomatic	938	100.0% (97.4%, 100.0%)	145/145	100.0% (99.5%, 100.0%)	793/793
	Asymptomatic	1526	100.0% (80.6%, 100.0%)	16/16	99.8% (99.4%, 99.9%)	1507/1510
	Total	2464	100.0% (97.7%, 100.0%)	161/161	99.9% (99.6%, 100.0%)	2300/2303
Specimen Type	Symptom Status	N	Positive Percent Agreement	Positive Percent Agreement	Negative Percent Agreement	Negative Percent Agreement
			Estimate (95% CI)	n/N	Estimate (95% CI)	n/N
Vaginal Swabs	Symptomatic	1115	91.7% (74.2%, 97.7%)	22/24	99.8% (99.3%, 99.9%)	1089/1091
	Asymptomatic	1357	100.0% (82.4%, 100.0%)	18/18	99.9% (99.5%, 100.0%)	1337/1339
	Total	2472	95.2% (84.2%, 98.7%)	40/42	99.8% (99.6%, 99.9%)	2426/2430
	Symptomatic	42	100.0% (83.9%, 100.0%)	20/20	100.0% (85.1%, 100.0%)	22/22

Archived Vaginal Swabs	Asymptomatic	48	100.0% (86.7%, 100.0%)	25/25	100.0% (85.7%, 100.0%)	23/23
	Total	90	100.0% (92.1%, 100.0)	45/45	100.0% (92.1%, 100.0%)	45/45
Overall Vaginal Swabs	Symptomatic	1157	95.5% (84.9%, 98.7%)	42/44	99.8% (99.3%, 100.0%)	1111/1113
	Asymptomatic	1405	100.0% (91.8%, 100.0%)	43/43	99.9% (99.5%, 100.0%)	1360/1362)
	Total	2562	97.7% (92.0%, 99.4%)	85/87	99.8% (99.6%, 99.9%)	2471/2475

CI: confidence interval

Table 22: MG - Clinical performance of cobas® liat CT/NG/MG compared with patient infected status by specimen type and symptom status

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

CI: confidence interval

6.3. Expected values for urogenital specimens

The positivity rate of the **cobas® liat** CT/NG/MG nucleic acid assay test for CT, NG, and MG observed during the study is shown for each specimen type, by collection site in Table 23 below.

Table 23: 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

6.3.1. Summary of Positive Predictive Value, Negative Predictive Value for Hypothetical Prevalence

The hypothetical PPVs and NPVs of **cobas® liat** CT/NG/MG derived from disease prevalences of 1% to 50% are shown in , Table 24, Table 25 and Table 26, respectively, for CT, NG, and MG.

Table 24: CT - Positive predictive value and negative predictive value for hypothetical CT prevalence

Specimen type for CNMA testing	Hypothetical Prevalence (%)	PPV (%)	NPV (%)
Male Urine	1	91.5	100.0
Male Urine	3	97.0	99.9
Male Urine	5	98.2	99.9
Male Urine	10	99.2	99.7
Male Urine	15	99.5	99.5
Male Urine	20	99.6	99.3
Male Urine	30	99.8	98.9
Male Urine	50	99.9	97.4
Vaginal Swabs	1	82.4	100.0
Vaginal Swabs	3	93.5	99.9
Vaginal Swabs	5	96.1	99.9
Vaginal Swabs	10	98.1	99.8
Vaginal Swabs	15	98.8	99.7
Vaginal Swabs	20	99.1	99.5
Vaginal Swabs	30	99.5	99.2
Vaginal Swabs	50	99.8	98.2

Note: NPV: negative predictive value; PPV: positive predictive value; PPA: positive percent agreement; NPA: negative percent agreement;

The PPV and NPV were calculated using the sensitivity/PPA and specificity/NPA of **cobas® liat** CT/NG/MG from the prospectively collected population.

Table 25: NG - Positive predictive value and negative predictive value for hypothetical NG prevalence

Specimen type for CNMA testing	Hypothetical Prevalence (%)	PPV (%)	NPV (%)
Male Urine	1	88.2	100.0
Male Urine	3	95.8	100.0
Male Urine	5	97.5	100.0
Male Urine	10	98.8	100.0
Male Urine	15	99.2	100.0
Male Urine	20	99.5	100.0
Male Urine	30	99.7	100.0
Male Urine	50	99.9	100.0
Vaginal Swabs	1	85.4	100.0
Vaginal Swabs	3	94.7	99.9
Vaginal Swabs	5	96.8	99.7
Vaginal Swabs	10	98.5	99.5
Vaginal Swabs	15	99.0	99.2
Vaginal Swabs	20	99.3	98.8
Vaginal Swabs	30	99.6	98.0
Vaginal Swabs	50	99.8	95.4

Note: NPV: negative predictive value; PPV: positive predictive value; PPA: positive percent agreement; NPA: negative

percent agreement;

The PPV and NPV were calculated using the sensitivity/PPA and specificity/NPA of **cobas® liat** CT/NG/MG from the prospectively collected population.

Table 26: MG - Positive predictive value and negative predictive value for hypothetical MG prevalence

Specimen type for CNMA testing	Hypothetical Prevalence (%)	PPV (%)	NPV (%)
Male Urine	1	56.2	100.0
Male Urine	3	79.7	99.9
Male Urine	5	87.0	99.8
Male Urine	10	93.4	99.7
Male Urine	15	95.7	99.5
Male Urine	20	96.9	99.3
Male Urine	30	98.2	98.8
Male Urine	50	99.2	97.2
Vaginal Swabs	1	30.4	100.0
Vaginal Swabs	3	57.2	99.8
Vaginal Swabs	5	69.4	99.7
Vaginal Swabs	10	82.7	99.5
Vaginal Swabs	15	88.4	99.1
Vaginal Swabs	20	91.5	98.8
Vaginal Swabs	30	94.9	98.0
Vaginal Swabs	50	97.7	95.4

Note: NPV: negative predictive value; PPV: positive predictive value;
The PPV and NPV were calculated using the sensitivity and specificity of **cobas® liat** CT/NG/MG from the prospectively collected population.

7. CONCLUSIONS

A comparison of the intended use, technological characteristics, and the results of non-clinical analytical and clinical performance studies demonstrate that **cobas® liat** CT/NG/MG nucleic acid test is **substantially equivalent** to the predicate devices.