cobas® liat CT/NG

nucleic acid test

For in vitro diagnostic use

For Rx Use Only
CLIA Complexity – WAIVED

cobas® liat CT/NG	P/N: 10030933190
cobas® liat CT, NG and MG control kit	P/N: 09449639190

Certificate of Waiver is required to perform the test in a CLIA Waived setting.

Laboratories with a Certificate of Waiver must follow the instructions for performing the test.

Intended use

The **cobas® liat** CT/NG 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) and *Neisseria gonorrhoeae* (NG) nucleic acid in male/female 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.

Summary

Infection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are leading bacterial causes of sexually transmitted infections worldwide. Although patients with these infections often present with clinical symptoms (such as dysuria, discharge, and/or pain), a significant proportion may be asymptomatic and therefore unsuspecting. If left untreated, infections caused by CT and NG can cause complications in the uterus, fallopian tubes, or ovaries and lead to long-term consequences such as pelvic inflammatory syndrome, ectopic pregnancy, infertility, and psychosocial harm,[1-3] exerting a severe burden on the health and economy of the world.[4,5] Urogenital infections are often asymptomatic and a high number of infected patients may not seek care. Moreover, patients often become reinfected if their sexual partners are not adequately diagnosed and treated.

A rapid and sensitive molecular-based point of care test can help to inform effective medical decision-making, optimize use of targeted therapies and antimicrobials, and facilitate infection control efforts.[6,7]

Test principle

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* and the pivNG and NGR9 of *Neisseria gonorrhoeae*. 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 sample to result time is approximately 20 minutes.

Precautions and warnings

- Before using the **cobas® liat** CT/NG nucleic acid test, the operator should carefully read all testing instructions, warnings, and precautions in the **cobas® liat** system User Guide.
- Treat all biological samples, including used **cobas® liat** CT/NG assay tubes and transfer pipettes, as if capable of transmitting infectious agents. All biological samples should be treated with universal precautions. Guidelines for sample handling are available from the U.S. Centers for Disease Control and Prevention, Clinical and Laboratory Standards Institute.[8,9]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Safety Data Sheets (SDS) are available on request from your local Roche representative.

- Use only the transfer pipettes contained in the **cobas® liat** transfer pipette pack. Use of alternative transfer pipettes may lead to invalid results.
- **cobas®** PCR Media contains guanidine hydrochloride. **Do not allow direct contact between guanidine hydrochloride and sodium hypochlorite (bleach) or other highly reactive reagents such as acids or bases. These mixtures can release a noxious gas.** If liquid containing guanidine hydrochloride is spilled, clean with soap and water. If the spilled liquid contains potentially infectious agents, **FIRST** clean the affected area with soap and water, and then with 0.5% sodium hypochlorite.
- Carefully adhere to the procedures specified in this Instructions for Use (IFU) document. Wear protective gloves and use PPE (personal protective equipment) as per local guidelines. Change gloves before removing transfer pipette from the **cobas® liat** transfer pipette pack and after handling each sample or control. After handling samples and kit reagents, remove gloves and wash hands thoroughly.
- Due to the high sensitivity of the assays run on the **cobas® liat** analyzer, contamination of the work area with previous samples may cause false positive results. Handle samples with caution. If spills occur on the **cobas® liat** analyzer, follow the appropriate instructions in the **cobas® liat** system User Guide to clean.

Sample collection, transport, and storage

See Table 4 for a list of collection kits for use with **cobas® liat** CT/NG. Follow the instructions for collecting all swab and urine samples in their respective collection kit IFU.

Urine samples

- Use only a urine collection cup (not provided) to collect the urine samples for **cobas® liat** CT/NG.
- Use only the **cobas®** PCR Urine Sample Kit to transfer urine samples for **cobas® liat** CT/NG.
- Transferred urine samples must show the top of the liquid level between the two black lines on the **cobas®** PCR Media tube label window. If the liquid level is above or below these lines, the sample has not been transferred properly and cannot be used for testing.

Vaginal swab samples (clinician-collected and self-collected)

- Use only the provided swab in the **cobas®** PCR Media Uni Swab Sample Kit to collect vaginal swab samples. **DO NOT** pre-wet swab in **cobas®** PCR Media before collection.
- Incoming swab sample tubes with no swabs or with two swabs have not been collected according to the instructions in their respective collection kit IFU and should not be tested.

Transport and storage

Transportation of collected samples must comply with all applicable regulations for the transport of etiologic agents.

- Urine and vaginal swab samples in **cobas®** PCR Media should be tested as soon as possible.
    - If needed, urine samples may be stored at 2-30°C for up to 3 hours after collection. If urine samples cannot be added to the assay tube within 3 hours of collection, urine samples may be stored at 2-8°C for up to 48 hours after collection.
    - If needed, vaginal swab samples may be stored at 2-30°C for up to 24 hours after collection. If vaginal swab samples cannot be added to the assay tube within 24 hours of collection, vaginal swab samples may be stored at 2-8°C for up to 72 hours after collection.

- Once samples have been transferred into a **cobas® liat** CT/NG assay tube, start the run on the **cobas® liat** analyzer as soon as possible but no later than 4 hours, with storage at room temperature (15-30°C).

Materials required, storage and handling

The materials provided for **cobas® liat** CT/NG can be found in Table 1 and Table 2. Reagent handling and storage can be found in Table 3. Materials required, but not provided, can be found in Table 4 and instrumentation and software required, but not provided, can be found in Table 5.

cobas® liat CT/NG reagents and controls

All unopened assay tubes and controls shall be stored as recommended in Table 1 to Table 3.

Table 1: cobas® liat CT/NG

cobas® liat CT/NG

Store at 2-8°C
20 tests (P/N 10030933190)
2 **cobas® liat** transfer pipette packs (12 pipettes/pack - P/N 09329676001)
1 Package Insert Barcode Card

Reagents in cobas® liat CT/NG assay tube	**Reagent ingredients**	**Safety symbol and warning**[a]
Internal Control	Tris buffer, EDTA, non-target related armored RNA construct containing primer and probe specific sequence regions (non-infectious RNA in MS2 bacteriophage), sodium azide	N/A
Liat Magnetic Particles	Magnetic Particles	N/A
Lysis Buffer	Guanidinium thiocyanate[b], Brij® 35, citric acid monohydrate	 **DANGER** H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H412: Harmful to aquatic life with long lasting effects. EUH032: Contact with acids liberates very toxic gas. EUH071: Corrosive to the respiratory tract. P273: Avoid release to the environment. P280: Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection. P301 + P330 + P331: IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. P305 + P351 + P338 + P310: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. 593-84-0 Guanidinium thiocyanate

Reagents in cobas® liat CT/NG assay tube	Reagent ingredients	Safety symbol and warning[a]
Wash Buffer	Sodium citrate dihydrate, methyl p-hydroxybenzoate	N/A
Elution Buffer	Tris, poly rA, EDTA, sodium azide	N/A
CT/NG Master Mix-1	Tricine, potassium acetate, potassium hydroxide, EDTA disodium dehydrate, DMSO, sodium azide, Tween-20, glycerol, rHSA, dATP, dCTP, dGTP, dUTP, Target and Internal Control primers, AmpErase (uracil-N glycosylase), Z05D C21 Reverse Transcriptase, aptamer	N/A
Co-Factor	Magnesium acetate, manganese acetate, sodium azide, acetic acid	N/A
CT/NG Master Mix-2	Tricine, potassium acetate, potassium hydroxide, EDTA disodium dehydrate, DMSO, sodium azide, Tween-20, rHSA, glycerol, Internal Control forward and reverse primers, forward and reverse target primers, target and Internal Control-specific fluorescent-labeled oligonucleotide probes, Z05 DNA polymerase, aptamer	N/A

[a] Product safety labeling primarily follows EU GHS guidance.

[b] Hazardous substance or mixture

Table 2: cobas® liat CT, NG and MG control kit

cobas® liat CT, NG and MG control kit

Store at 2-8°C
(P/N 09449639190)
1 Control Kit Barcode Card

Kit components	Reagent ingredients	Quantity per kit	Safety symbol and warning[a]
cobas® liat CT, NG and MG positive control tube (P/N 09449647001)	Sodium Azide, Poly rA, EDTA, Tris, Non-infectious plasmid DNA (microbial) containing *C. trachomatis* sequence, Non-infectious plasmid DNA (microbial) containing *N. gonorrhoeae* sequence, Non-infectious armored RNA (microbial) containing *M. genitalium* sequence	3 x 0.3 mL	N/A
cobas® liat CT, NG and MG negative control (NEG BUF) tube (P/N 09587373001)	Tris buffer, sodium azide, EDTA, Poly rA	3 x 0.3 mL	N/A

[a] Product safety labeling primarily follows EU GHS guidance.

Table 3: Materials provided

P/N	Material description	Quantity	Storage temperature	Storage time
10030933190	**cobas® liat** CT/NG	20 tests	2-8°C*	Stable until the expiration date indicated
09449639190	**cobas® liat** CT,NG and MG control kit	3 sets	2-8°C	Stable until the expiration date indicated

Note: Do not freeze reagents.

*For short-term storage, **cobas® liat** CT/NG assay tube kits may be stored for up to 3 days at room temperature. Kits should be labeled with the start date of room temperature storage and disposed of if not used within 3 days. The **cobas® liat** transfer pipette pack may be stored at room temperature following first removal from the kit.

Table 4: Materials required but not provided

P/N	Material description
05170486190	Urine Collection Kit: **cobas®** PCR Urine Sample Kit
07958030190	Vaginal Swab Collection Kit: **cobas®** PCR Media Uni Swab Sample Kit

Table 5: Instrumentation and software required but not provided

Equipment and Software
cobas® liat analyzer (P/N 07341920190) Including **cobas® liat** system software version 3.4 or higher
cobas® liat CT/NG script (CNDA) v1.0 (IVD) or higher

Note: For additional information regarding the **cobas® liat** analyzer, please refer to the **cobas® liat** system User Guide.

Test procedure

Procedural notes

- Do not use **cobas® liat** CT/NG assay tube and **cobas® liat** CT, NG and MG control kit after their expiry dates.
- Do not open individual assay tube packaging until operator is ready to perform testing.
- Do not reuse assay tubes, positive and negative controls, and transfer pipettes. They are for single use only.
- Do not use a damaged **cobas® liat** CT/NG assay tube. Do not use a **cobas® liat** CT/NG assay tube that has been dropped after removal from its foil pouch.
- Ensure there is no sign of leakage from the collection tube prior to running the test.
- Ensure any additional labels are only placed on the back of the tube sleeve or around the side of the cap, do not place labels over barcodes or over the top of the assay tube cap.
- Do not open the cap of the **cobas® liat** CT/NG assay tube during or after the run on the **cobas® liat** analyzer.
- Dispose of all materials that have come in contact with samples and reagents in accordance with country, state, and local regulations.
- Do not invert the assay tube and shake.

Procedural limitations

- **cobas® liat** CT/NG has been evaluated only for use in combination with the **cobas® liat** CT, NG and MG control kit and this Instructions For Use document. Modifications to these procedures may alter the performance of the test.
- Reliable results are dependent on adequate specimen collection, transport, storage, and processing. Failure to observe

proper procedures in any one of these steps can lead to incorrect results.

- A negative test result for CT or NG does not preclude the possibility of infection. If clinical symptoms persist, additional testing should be performed.
- Assay performance has not been evaluated in patients younger than 15 years of age.
- Results should be interpreted in conjunction with the patient medical history and/or clinical signs and symptoms, and the results of other diagnostic tests.
- This test is intended to be used for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in male/female urine and vaginal swabs in **cobas®** PCR Media (Roche Molecular Systems, Inc.). Testing of other sample or media types may lead to inaccurate results.
- Invalid results may be obtained if there is insufficient sample volume or if the specimen contains inhibitory substances that prevent nucleic acid target extraction and/or amplification and detection.
- False negative results may occur if a specimen is improperly collected, transported, or handled; or if there is insufficient nucleic acid to be detected.
- A vaginal swab (self-or clinician-collected) is the preferred specimen type for CT and NG testing in females due to the higher sensitivity compared to female urine. If female urine is collected and negative results are obtained for any analyte, and infection is still suspected, consider testing from a vaginal swab sample.
- Though rare, mutations within the targeted regions of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) covered by the primers or probes used in the **cobas® liat** CT/NG test may result in failure to detect the presence of the bacterium.
- Assay performance was not established in immunocompromised patients.
- 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.

cobas® liat CT/NG assay tube Lot Validation

Before using a new lot of **cobas® liat** CT/NG assay tubes, a Lot Validation procedure must be performed on the **cobas® liat** analyzer to validate the **cobas® liat** CT/NG assay tube lot at your site. The procedure includes running a negative control (NEG BUF) and a positive control.

Note: *Refer to the **cobas® liat** system User Guide for detailed operating instructions.*

Materials needed for Lot Validation

From **cobas® liat** CT/NG assay tube kit:	From **cobas® liat** CT, NG and MG control kit:
□ 2 **cobas® liat** CT/NG assay tubes	□ 1 **cobas® liat** CT, NG and MG negative control (NEG BUF) tube
□ 2 transfer pipettes	□ 1 **cobas® liat** CT, NG and MG positive control tube
□ package insert barcode card	□ negative/positive control barcode card*

Note:* The negative and positive control barcodes pertaining to the **cobas® liat CT/NG test are in Section 2 of the negative/positive control barcode card.

Assay tube Lot Validation workflow

1	Press the power on/off button to start the **cobas® liat** analyzer.
2	Choose **"Logon**". Enter user name and password when prompted, choose **"Enter".**
3	From the **Main** menu, choose **Assay Menu**. From the Assay Menu, choose **[New Lot]**.
4	Choose **Scan**, and scan the Package Insert barcode from the package insert barcode card.
5	Choose **Scan** and scan the negative control barcode from the barcode card (Section 2) included with the control kit. ***Note: Ensure to match the lot number on the control tube with lot on the negative/positive control barcode card***
6	Remove the cap of the **cobas® liat** CT/NG assay tube. Using the transfer pipette provided in the **cobas® liat** transfer pipette pack, firmly squeeze the bulb of the transfer pipette, lower it into the liquid in the negative control (NEG BUF) tube and release the bulb to slowly draw up the control and slowly transfer the control into the opening of the assay tube by squeezing the bulb. Recap the assay tube and dispose of the transfer pipette and control tube. ***Note: Only use the transfer pipette provided in the cobas® liat transfer pipette pack to transfer controls and samples into the cobas® liat CT/NG assay tube.*** ***Note: Reseal the cobas® liat transfer pipette pack immediately after removing the necessary pipette(s).*** ***Note: Do not puncture the cobas® liat CT/NG assay tube or the seal at the bottom of the sample compartment. If either of these are damaged, dispose both the cobas® liat CT/NG assay tube and the transfer pipette, and restart the testing procedure with a new cobas® liat CT/NG assay tube and pipette.***
7	Choose **Scan**, and scan the **cobas® liat** CT/NG assay tube barcode. Remove the assay tube sleeve and insert the assay tube into the analyzer tube entry door until the tube clicks into place. Processing begins automatically.
8	Once the test is complete, if the **cobas® liat** analyzer displays **"Negative control result accepted."**, choose **Confirm.** Then, remove and dispose the **cobas® liat** CT/NG assay tube. Choose **Back** and repeat Steps 5-8 for the positive control. ***Note: In Step 5, Scan the positive control barcode from the negative/positive control barcode card.*** When the positive control result is accepted, you can begin using the lot. ***Note: If the result is rejected, repeat the control run. If repeated control run does not produce the expected result, contact your local Roche representative.***
9	***Optional*:** To transfer the lot information to the other analyzers at your site refer to the **cobas® liat** system User Guide.

cobas® liat CT/NG sample testing workflow

Materials needed for a sample run

- □ 1 **cobas® liat** CT/NG assay tube
- □ 1 transfer pipette
- □ 1 sample in **cobas®** PCR Media tube

1	Press the power on/off button to start the **cobas® liat** analyzer.
2	Choose **"Logon**". Enter user name and password when prompted, choose **"Enter"**.
3	Obtain clinical sample, **cobas® liat** CT/NG assay tube, and transfer pipette provided in the **cobas® liat** transfer pipette pack.
4	From the **Main** menu, choose **Run Assay**. Then **Scan** the **cobas® liat** CT/NG assay tube barcode.
5	**Scan** the sample ID or choose **Enter** to enter the ID manually. ***Note: Depending on analyzer configuration, if required to confirm the received patient information, choose the Confirm button.***
6	Remove the cap of the **cobas® liat** CT/NG assay tube. Using the transfer pipette provided in the **cobas® liat** transfer pipette pack, firmly squeeze the bulb of the transfer pipette, lower it into the liquid in the sample collection media tube and release the bulb to draw up the sample and slowly transfer the sample into the opening of the assay tube by squeezing the bulb. Recap the assay tube and dispose of the transfer pipette. ***Note: Only use the transfer pipette provided in the cobas® liat transfer pipette pack to transfer controls and samples into the cobas® liat CT/NG assay tube.*** ***Note: Reseal the cobas® liat transfer pipette pack immediately after removing the necessary pipette(s).*** ***Note: Do not puncture the cobas® liat CT/NG assay tube or the seal at the bottom of the sample compartment. If either of these are damaged, dispose both the cobas® liat CT/NG assay tube and the transfer pipette, and restart the testing procedure with a new cobas® liat CT/NG assay tube and pipette.***
7	Choose **Scan**, and rescan the **cobas® liat** CT/NG assay tube barcode. Remove the assay tube sleeve and insert the assay tube into the analyzer tube entry door until the tube clicks into place. Processing begins automatically. ***Note: Processing of the assay tube must begin within 4 hours of sample addition to the cobas® liat CT/NG assay tube (step 5).***
8	When the assay run is complete, remove and dispose the used **cobas® liat** CT/NG assay tube.
9	Choose the **Report** button to view the result report for validity.* ***Note: For result interpretation please refer to Interpretation of results section.***

*Refer to **cobas® liat** system User Guide for details of result uploading to LIS.

Note: When performing additional positive control and/or negative control runs, in accordance with local, state, federal and/or accrediting organization requirements, follow the procedures outlined under the section "**cobas® liat** CT/NG sample testing workflow". In step 5, be sure to use the provided control barcodes included in **cobas® liat** CT, NG and MG control kit to scan as sample ID barcode. Interpretation of results for **cobas® liat** CT/NG when running additional **cobas® liat** CT, NG and MG positive control or negative control are shown in the "Interpretation of results" section (Table 6). Using barcodes other than the control barcodes provided may lead to incorrect control results.

Interpretation of results

Table 6: Interpretation of results of **cobas® liat** CT/NG when running "Lot Validation" procedure or additional control runs

cobas® liat analyzer Display	**Result Interpretation**
Negative Control Valid	**Negative Control Valid** Control is negative for the presence of CT/NG.
Negative Control Invalid. Repeat Run*	**Negative Control Invalid** Result is Invalid. The Negative Control should be re-tested to obtain valid result. Repeat run.
Positive Control Valid	**Positive Control Valid** Control is positive for the presence of CT/NG.
Positive Control Invalid. Repeat Run*	**Positive Control Invalid** Result is Invalid. The positive control should be re-tested to obtain valid result. Repeat run.

If the repeated run is still invalid, contact your Roche representative.

*For additional control runs, "Repeat Run" will not be part of the result report in the case of an invalid result.

Table 7: Interpretation of results of **cobas® liat** CT/NG when running a sample

cobas® liat analyzer Display	**Result Interpretation**
CT Not Detected	**Valid Negative test for CT** (no CT detected)
CT Detected	**Valid Positive test for CT** (CT present)
CT Invalid	**Presence or absence of CT could not be determined. Repeat assay with same sample.**
NG Not Detected	**Valid Negative test for NG** (no NG detected)
NG Detected	**Valid Positive test for NG** (NG present)
NG Invalid	**Presence or absence of NG could not be determined. Repeat assay with same sample.**
Assay Invalid	**Presence or absence of or CT or NG could not be determined. Repeat assay with same sample.**
Assay Aborted by System	**Run failed or aborted by system. Repeat assay with same sample.**
Assay aborted by script: Script aborted	**Run failed or aborted by script. Repeat assay with same sample.**
Assay Aborted by User	**Run aborted by user.**

Non-clinical performance evaluation

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) and *Neisseria gonorrhoeae* (NG, Strains 2948 and 891). The CT and NG 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 8 and Table 9 for CT and NG respectively as the target concentration which can be detected in ≥ 95% of the replicates for all lots.

Table 8: 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 9: 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

Inclusivity

Inclusivity was performed for an additional 15 CT serovars and 43 NG strains using one lot of reagents. Testing was performed using CT and NG 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 10 and Table 11 for CT and NG respectively.

Table 10: 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 11: 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

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

Analytical specificity/cross reactivity

A panel of 181 strains of bacteria, fungi and viruses, including those commonly found in patient specimens, as well as 52 representative strains of non-*gonorrhoeae Neisseria* species and other phylogenetically unrelated organisms, were tested to assess analytical specificity. The organisms listed in Table 12 were spiked at concentrations of $\geq 1 \times 10^6$ units/mL* for bacteria or fungi and $\geq 1 \times 10^5$ 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 and NG 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.

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

Table 12: Microorganisms tested for analytical specificity/cross reactivity

Acholeplasma laidlawii	*Eikenella corrodens*	*Mobiluncus curtisii*	*Peptostreptococcus anaerobius*
Acholeplasma oculi[1,3]	*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[1,3]	*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*[1,3]	*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)[2]	*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*[1,3]

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*	-

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

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

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

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 13. Testing was executed using pooled clinical specimens spiked with potential interferents at levels expected from normal patient usage. Interferents were tested in CT/NG negative specimen pools as well as in positive specimen pools spiked with CT/NG at ~3x LoD for each specimen type using one lot of reagents. Five replicates each of CT/NG negative sample and CT/NG 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 13.

Table 13: 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-Itch 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
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 14. 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 negative specimen pools as well as in positive specimen pools spiked with CT/NG at ~3x LoD for each relevant specimen type using one lot of reagents. Five replicates each of CT/NG negative sample and CT/NG 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 14.

Table 14: 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	-

Competitive inhibition

To assess competitive inhibition between CT and NG, a 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.

Reproducibility studies

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 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 15 and Table 16 show the site-to-site Reproducibility Study results for **cobas® liat** CT/NG by sample type and panel member concentration, respectively for CT and NG.

Table 15: Summary CT of site-to-site reproducibility results with **cobas® liat** CT/NG

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 16: Summary NG of site-to-site reproducibility results with **cobas® liat** CT/NG

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	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 17 and Table 18 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, respectively for CT and NG.

Table 17: 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 by sample type and positive panel member concentration

-				Between Site	Between Site	Between Lot	Between Lot	Between Day	Between Day	Between Operator / Run	Between Operator / Run	Within-Run	Within-Run	Total	Total
Sample Type	Panel Member Concentration	n/N[a]	Mean Ct	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	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 18: 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 by sample type and positive panel member concentration

-				Between Site	Between Site	Between Lot	Between Lot	Between Day	Between Day	Between Operator / Run	Between Operator / Run	Within - Run	Within - Run	Total	Total
Sample Type	**Panel Member Concentration**	**n/N[a]**	**Mean Ct**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**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.

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

Table 19: 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%
1-2x LoD	2	44/44	100.0%
1-2x LoD	3	45/45	100.0%
1-2x LoD	4	44/44	100.0 %
1-2x LoD	5	45/45	100.0%
1-2x LoD	6	45/45	100.0%
3-5x LoD	1	45/45	100.0%
3-5x LoD	2	45/45	100.0%
3-5x LoD	3	45/45	100.0%
3-5x LoD	4	45/45	100.0%
3-5x LoD	5	45/45	100.0%
3-5x LoD	6	44/44	100.0%
Negative	1	43/44	97.7%
Negative	2	45/45	100.0%
Negative	3	45/45	100.0%
Negative	4	45/45	100.0%
Negative	5	45/45	100.0%
Negative	6	44/44	100.0%

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

Table 20 shows the supplemental Reproducibility Study for **cobas® liat** CT/NG 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 20: CT - Overall mean estimate, standard deviations, and coefficients of variation (%) for cycle threshold values and expected concentration for **cobas® liat** CT/NG by positive panel member concentration in urine

-			Between Instrument	Between Instrument	Bet-ween Lot	Bet-ween Lot	Bet-ween Day	Bet-ween Day	Bet-ween Operator /Run	Bet-ween Operator /Run	Within-Run	Within-Run	Total	Total
Panel Member Concentration	**n/N[a]**	**Mean Ct**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**	**SD**	**CV%**
1x-2xLOD	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
3x-5xLOD	269/269	33.7	0.00	0.00	0.00	0.00	0.00	0.00	0.46	1.35	1.07	3.19	1.17	3.47

Note: Ct = cycle threshold, CT=*Chlamydia trachomatis*, CV(%) = percent coefficient of variation, LoD = Limit of Detection, 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.

Clinical performance evaluation

Clinical study

The clinical utility and performance of **cobas® liat** CT/NG 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 2 analytes. A result for PIS (for male urine urine) or a CCA (for vaginal swabs and female urine) was generated for CT and NG. Male urine, vaginal swabs, and female urine 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 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® liat** CT/NG 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 nucleic acid test. Vaginal swab specimen for the **cobas® liat** CT/NG nucleic acid test was either collected by clinician or self-collected. Female subjects also provided a urine specimen that was aliquoted into the respective manufacturers' collection devices and **cobas®** PCR Media.

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 and NG with the investigational and the reference comparator NAATs. All tests were run according to the respective IFUs.

The clinical performance of **cobas® liat** CT/NG 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 reference 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 21 below shows the PIS and CCA algorithm for each analyte.

Table 21: Determination of the PIS/CCA result for CT and NG, respectively

NAAT 1	NAAT 2	NAAT 3	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
+	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 "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 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 were calculated separately for CT and NG.

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).

A supplemental study was conducted to evaluate the performance of **cobas® liat** CT/NG for the assessment of detecting CT in female urine. 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. In this study, comparator testing and final evaluation was determined by comparing results from **cobas® liat** CT/NG to a CCA as described above and shown in Table 21. This supplemental set of data for CT was combined with the female urine data from the aforementioned study. The performance data tables below (Table 23) will be labeled to indicate that the performance was generated as part of the supplemental study.

Additionally, the **cobas® liat** CT/NG performance for the detection NG, also from female urine is presented below (Table 25). Similarly, the CCA was determined from 3 comparator NAATs as shown in Table 21. This set of data was part of the original study described above.

A vaginal swab (self-collected or clinician-collected) is the preferred specimen type for CT and NG testing in females due to a higher sensitivity when compared to urine. If a female urine is used and CT and/or NG testing is negative, further testing with a vaginal swab may be indicated if *C. trachomatis* and/or *N. gonorrhoeae* infection is strongly suspected.

Analysis of both studies show that the **cobas® liat** CT/NG 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.

Performance results

Sensitivity/PPA and specificity/NPA of **cobas® liat** CT/NG as defined by the PIS/CCA results are presented by gender, sample type, and symptom status in Table 22 and Table 23 for CT, and Table 24 and Table 25 for NG.

Upon initial testing, the **cobas® liat** CT/NG invalid rate was 0.6% and after retesting the final invalid rate was 0.2%.

Table 22: CT - Clinical performance of **cobas® liat** CT/NG compared with PIS/CCA by specimen type and symptom status - prospectively collected specimens

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
Male Urine	Asymptomatic	1488	96.4% (87.7%, 99.0%)	53/55	99.9% (99.6%, 100.0%)	1432/1433
Male Urine	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 Estimate (95% CI)**	**Positive Percent Agreement n/N**	**Negative Percent Agreement Estimate (95% CI)**	**Negative Percent Agreement n/N**
Vaginal Swabs	Symptomatic	1116	98.4% (91.3%, 99.7%)	60/61	99.7% (99.2%, 99.9%)	1052/1055
Vaginal Swabs	Asymptomatic	1357	97.9% (89.1%, 99.6%)	47/48	99.8% (99.4%,100.0%)	1307/1309
Vaginal Swabs	Total	2473	98.2% (93.6%, 99.5%)	107/109	99.8% (99.5%, 99.9%)	2359/2364

CI: confidence interval

Table 23: CT – Clinical Performance of **cobas® liat®** CT/NG compared with CCA by symptom status - Female Urine

Study	Symptom Status	N	Positive Percent Agreement Estimate (95% CI)	Positive Percent Agreement n/N	Negative Percent Agreement Estimate (95% CI)	Negative Percent Agreement n/N
Supplemental Study	Symptomatic	312	100.0% (81.6%, 100.0%)	17/17	99.3% (97.6%, 99.8%)	293/295
Supplemental Study	Asymptomatic	439	93.8% (71.7%, 98.9%)	15/16	99.3% (97.9%, 99.8%)	420/423
Supplemental Study	Overall	751	97.0% (84.7%, 99.5%)	32/33	99.3% (98.4%, 99.7%)	713/718
Original LIA-497 Study FU Subset	Symptomatic	1113	93.0% (83.3%, 97.2%)	53/57	99.8% (99.3%, 99.9%)	1054/1056
Original LIA-497 Study FU Subset	Asymptomatic	1346	97.6% (87.4%, 99.6%)	40/41	99.8% (99.3%, 99.9%)	1302/1305
Original LIA-497 Study FU Subset	Overall	2459	94.9% (88.6%, 97.8%)	93/98	99.8% (99.5%, 99.9%)	2356/2361
Combined	Symptomatic	1425	94.6% (86.9%, 97.9%)	70/74	99.7% (99.2%, 99.9%)	1347/1351
Combined	Asymptomatic	1785	96.5% (88.1%, 99.0%)	55/57	99.7% (99.2%, 99.8%)	1722/1728
Combined	Overall	3210	95.4% (90.4%, 97.9%)	125/131	99.7% (99.4%, 99.8%)	3069/3079

CI: confidence interval

Table 24: NG - Clinical performance of **cobas® liat** CT/NG 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	813	100.0% (94.7%, 100.0%)	68/68	100.0% (99.5%, 100.0%)	745/745
Male Urine	Asymptomatic	1488	100.0% (74.1%, 100.0%)	11/11	99.8% (99.4%, 99.9%)	1474/1477
Male Urine	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
Archived Male Urine	Asymptomatic	38	100.0% (56.6%, 100.0%)	5/5	100.0% (89.6%, 100.0%)	33/33
Archived Male Urine	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
Overall Male Urine	Asymptomatic	1526	100.0% (80.6%, 100.0%)	16/16	99.8% (99.4%, 99.9%)	1507/1510
Overall Male Urine	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 Estimate (95% CI)**	**Positive Percent Agreement n/N**	**Negative Percent Agreement Estimate (95% CI)**	**Negative Percent Agreement n/N**
Vaginal Swabs	Symptomatic	1115	91.7% (74.2%, 97.7%)	22/24	99.8% (99.3%, 99.9%)	1089/1091
Vaginal Swabs	Asymptomatic	1357	100.0% (82.4%, 100.0%)	18/18	99.9% (99.5%, 100.0%)	1337/1339
Vaginal Swabs	Total	2472	95.2% (84.2%, 98.7%)	40/42	99.8% (99.6%, 99.9%)	2426/2430
Archived Vaginal Swabs	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
Archived Vaginal Swabs	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
Overall Vaginal Swabs	Asymptomatic	1405	100.0% (91.8%, 100.0%)	43/43	99.9% (99.5%, 100.0%)	1360/1362)
Overall Vaginal Swabs	Total	2562	97.7% (92.0%, 99.4%)	85/87	99.8% (99.6%, 99.9%)	2471/2475

CI: confidence interval

Table 25: NG - Clinical performance of **cobas® liat®** CT/NG compared with CCA by symptom status - Female Urine

Symptom Status	N	Positive Percent Agreement Estimate (95% CI)	Positive Percent Agreement n/N	Negative Percent Agreement Estimate (95% CI)	Negative Percent Agreement n/N
Symptomatic	1111	100.0% (83.9%, 100.0%)	20/20	99.9% (99.5%, 100.0%)	1090/1091
Asymptomatic	1347	100.0% (81.6%, 100.0%)	17/17	99.9% (99.6%, 100.0%)	1329/1330
Overall	2458	100.0% (90.6%, 100.0%)	37/37	99.9% (99.7%, 100.0%)	2419/2421

CI: confidence interval

Expected values for urogenital specimens

The positivity rate of the **cobas® liat** CT/NG nucleic acid assay test for CT, and NG observed during the study is shown for each specimen type, by collection site in Table 26 below and from the Supplemental Female Urine CT study in Table 27.

Table 26: Positivity of CT/NG as Determined by the **cobas® liat** CT/NG nucleic acid test by Specimen Type and Clinical Site

Collection Site	CT Male Urine	CT Vaginal Swab	CT Female Urine	NG Male Urine	NG Vaginal Swab	NG Female Urine
1	8.7% (30/343)	9.2% (14/152)	6.6% (10/151)	11.0% (38/346)	3.3% (5/152)	2.0% (3/151)
2	2.6% (9/346)	6.2% (15/241)	5.4% (13/240)	1.7% (6/346)	3.7% (9/241)	3.8% (9/240)
3	11.9% (18/151)	8.2% (30/366)	7.4% (27/365)	6.6% (10/151)	0.55% (2/364)	0.6% (2/362)
4	11.2% (12/107)	0.63% (1/160)	0.0% (0/161)	9.3% (10/107)	1.25% (2/160)	1.2% (2/161)
5	0.0% (0/4)	NC	NC	0.0% (0/4)	NC	NC
6	0.9% (1/117)	1.2% (1/85)	2.4% (2/83)	0.0% (0/118)	1.2% (1/85)	0.0% (0/83)
7	5.3% (3/57)	5.7% (2/35)	7.5% (3/40)	1.8% (1/57)	2.9% (1/35)	2.5% (1/40)
8	0.0% (0/80)	0.0% (0/19)	0.0% (0/17)	2.5% (2/80)	0.0% (0/19)	0.0% (0/17)
9	1.3% (6/468)	1.9% (10/527)	1.9% (10/524)	0.4% (2/469)	2.3% (12/528)	1.5% (8/526)
10	0.5% (1/198)	1.4% (5/347)	0.9% (3/348)	1.0% (2/198)	0.86% (3/347)	0.9% (3/348)
11	17.1% (18/105)	5.6% (17/305)	4.6% (14/304)	4.8% (5/105)	2.0% (6/305)	2.3% (7/304)
12	3.5% (10/289)	8.8% (12/136)	9.6% (13/136)	1.7% (5/289)	1.5% (2/136)	1.5% (2/136)
13	6.5% (2/31)	5.0% (5/100)	4.0% (4/101)	3.2% (1/31)	1.0% (1/100)	2.0% (2/101)

Note: two subjects were born male, but were evaluated using self-collected vaginal swabs.

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

Table 27: Positivity of CT as Determined by the **cobas® liat** CT/NG nucleic acid test from Supplement Female Urine Study

Collection Site	CT Female Urine
14	4.9% (37/751)

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

The hypothetical PPVs and NPVs of **cobas® liat** CT/NG derived from disease prevalences of 1% to 50% are shown in Table 28 and Table 29 for CT, and Table 30 and Table 31 for NG.

Table 28: 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 from the prospectively collected population.

Table 29: CT - Positive predictive value and negative predictive value for hypothetical CT prevalence (original and supplemental studies) – Female Urine

Hypothetical Prevalence (%)	PPV (%)	NPV (%)
1	74.8	100.0
3	90.1	99.9
5	93.9	99.8
10	97.0	99.5
15	98.1	99.2
20	98.7	98.9
30	99.2	98.1
50	99.7	95.6

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 PPA and NPA of **cobas® liat** CT/NG from the prospectively collected population.

Table 30: 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 from the prospectively collected population.

Table 31: NG - Positive predictive value and negative predictive value for hypothetical NG prevalence – Female Urine

Hypothetical Prevalence (%)	PPV (%)	NPV (%)
1	92.4	100.0
3	97.4	100.0
5	98.5	100.0
10	99.3	100.0
15	99.5	100.0
20	99.7	100.0
30	99.8	100.0
50	99.9	100.0

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 from the prospectively collected population.

Failure codes

The result report may contain failure codes as described in Table 32, depending on potential run failures. For any questions, please contact your Roche Service representative.

Table 32: Failure codes and definitions

Failure Codes	Sample	Negative Control	Positive Control
g0/g1	IC out of range.	IC out of range.	IC out of range.
x4	CT/NG target out of range.	N/A	CT/NG target out of range.
FP	N/A	CT/NG target out of range.	N/A
x5	Low sample volume.	Low sample volume.	N/A

CLIA Waiver Study

Clinical performance characteristics of the **cobas® liat** CT/NG test were evaluated in a multi-site prospective study during December 2022 to August 2023 in the U.S. Thirteen (13) collection sites and two (2) reference laboratories throughout the U.S. participated in the clinical study. All the sites qualified as representative of CLIA waived intended use sites for this device.

Operators at all 13 external sites were chosen to represent the intended users. From these sites, 48 **cobas® liat** operators took part in study testing and were chosen to represent typical POC operators (e.g., nurses, medical assistants). Of these 48 operators, 43 were in CLIA waived sites.

Please refer to the clinical study section for the clinical performance data.

A Device Performance with Analyte Concentrations Near Cutoff study was performed to assess the capability of CLIA waived site intended operators to test true negative and weak positive samples and obtain accurate results. This was evaluated as a part of the reproducibility study.

Two operators at each site each tested 1 panel per specimen type per day. All replicates for each panel member were always tested on the same analyzer. For each panel member, approximately 270 results were produced.

Table 33: Results for near cutoff study

Specimen Type	Panel Member Concentration	Site 1 Agreement with Expected Results	Site 2 Agreement with Expected Results	Site 3 Agreement with Expected Results	Overall Agreement with Expected Results
CT - 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%)
CT - 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%)
CT - 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%)
CT - 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%)
NG - 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%)
NG - 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%)
NG - 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%)
NG - 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%)

Near cutoff assessment was also performed for the supplemental Precision Study. A total of 810 evaluable tests on urine panel members was evaluated.

Table 34: Results for near cutoff study for CT in urine from supplemental precision study

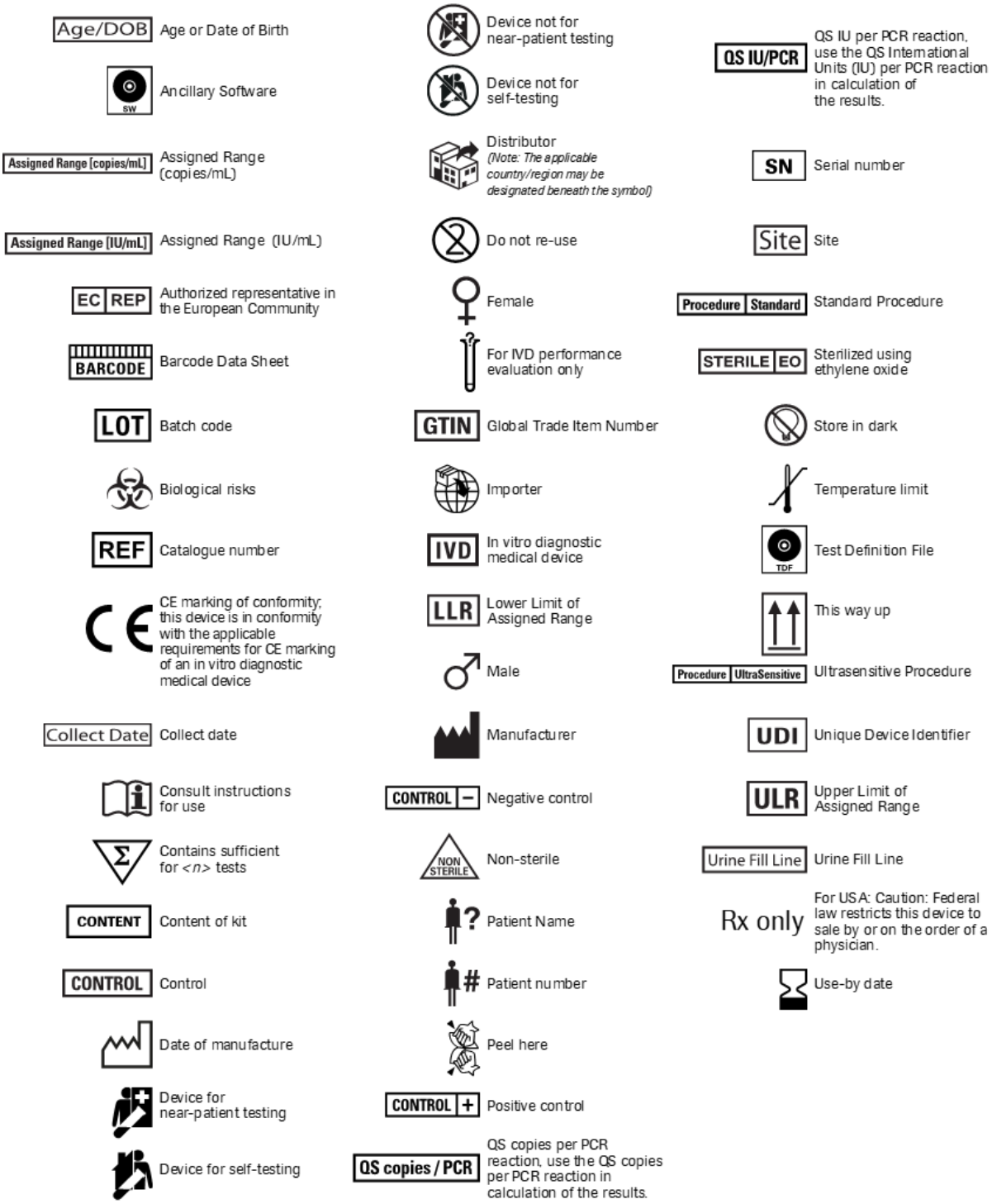
Operator	Panel Member Concentration	n/N[a]	Agreement with Expected Results (%)
1	1-2x LoD	44/45	97.8%
2	1-2x LoD	44/44	100.0%
3	1-2x LoD	45/45	100.0%
4	1-2x LoD	44/44	100.0 %
5	1-2x LoD	45/45	100.0%
6	1-2x LoD	45/45	100.0%
1	Negative	43/44	97.7%
2	Negative	45/45	100.0%
3	Negative	45/45	100.0%
4	Negative	45/45	100.0%
5	Negative	45/45	100.0%
6	Negative	44/44	100.0%

Using risk analysis as a guide, analytical flex studies were conducted. The studies demonstrated that the test is insensitive to stresses of environmental conditions and potential user errors.

Additional information

Symbols

The following symbols are used in labeling for Roche PCR assays.



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Document revision

Document Revision Information	
Doc Rev. 2.0 06/2026	Inclusion of the female urine sample type, based on supplemental clinical trial results for *Chlamydia trachomatis*. Removal of the limitation for potential false negatives, due to an algorithm change to correct calls (ECR 400292944). General corrections for consistent wording throughout the document. Please contact your local Roche Representative if you have any questions.