Rx Only

cobas® SARS-CoV-2

Nucleic acid test for use on the cobas® Liat® System

For in vitro diagnostic use

CLIA Complexity: WAIVED

cobas® SARS-CoV-2	P/N: 09408592190
cobas® SARS-CoV-2 Quality Control Kit	P/N: 09408835190

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Intended use

The **cobas**® SARS-CoV-2 Nucleic acid test for use on the **cobas**® Liat® System (**cobas**® SARS-CoV-2) is an automated, real-time reverse transcriptase polymerase chain reaction (RT-PCR) test intended for the rapid in vitro qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in anterior nasal (nasal) and nasopharyngeal swab specimens collected from individuals with signs and symptoms of respiratory tract infection (i.e., symptomatic). Additionally, this test is intended to be used with nasal and nasopharyngeal swab specimens collected from individuals without signs and symptoms suspected of COVID-19 (i.e., asymptomatic).

The **cobas**® SARS-CoV-2 performed on the **cobas**® Liat® System is intended for use as an aid in the diagnosis of COVID-19 if used in conjunction with other clinical, epidemiologic, and laboratory findings. SARS-CoV-2 RNA is generally detectable in nasal and nasopharyngeal swab specimens during the acute phase of infection.

Positive results are indicative of the presence of SARS-CoV-2 RNA. Positive results do not rule out co-infection with other microorganisms.

A negative result from an asymptomatic individual is presumptive. Additionally, a negative result obtained with a nasal swab collected from an asymptomatic patient should be followed up by testing at least twice over three days with at least 48 hours between tests. Negative results do not preclude SARS-CoV-2 infection.

The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

This test is intended for prescription use only and can be used in Point-of-Care settings.

Summary and explanation of the test

Background

Coronavirus disease 2019 (COVID-19) is a respiratory illness caused by a novel human coronavirus, named SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) by the World Health Organization.[1-3] COVID-19 has been declared a public health emergency of international concern and is the first pandemic caused by coronavirus.[4,5] COVID-19 is a potentially fatal infection that results in significant worldwide morbidity and mortality.[6]

Rapid and accurate diagnosis of COVID-19 infection is important in individuals suspected of a respiratory infection or in individuals who require screening for COVID-19 infection. The clinical manifestation of COVID-19 can range from asymptomatic or mild “influenza-like” illness (such as fever, cough, shortness of breath, or myalgia) in a majority of individuals to more severe and life-threatening disease.[7-9] Rapid and accurate detection of SARS-CoV-2 can help to inform time-critical medical decision-making, facilitate infection control efforts, promote efficient resourcing, optimize use of targeted therapies and antimicrobials, and reduce ancillary testing or procedures.[10,11]

Explanation of the test

cobas® SARS-CoV-2 assay uses real-time reverse transcriptase polymerase chain reaction (RT-PCR) technology to rapidly (approximately 20 minutes) detect SARS-CoV-2 virus from nasopharyngeal and nasal swabs. The automation, small footprint, and easy-to-use interface of the **cobas**® Liat® System enable performance of this test to occur at the POC or in a clinical laboratory setting.

Principles of the procedure

The **cobas**® SARS-CoV-2 assay 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 RT-PCR assays. The assay targets both the ORF1 a/b non-structural region and structural nucleocapsid protein (N) gene that are unique to SARS-CoV-2. An Internal Process Control (IPC) is also included. The IPC is present to control for adequate processing of the target virus through steps of sample purification, nucleic acid amplification, and to monitor the presence of inhibitors in the RT-PCR processes.

Reagents and materials

The materials provided for **cobas**® SARS-CoV-2 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 Table 5.

Refer to the **Reagents and materials** section and the **Precautions and handling requirements** section for the hazard information for the product.

cobas® SARS-CoV-2 reagents and controls

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

Table 1 cobas® SARS-CoV-2

cobas® SARS-CoV-2

Store at 2-8°C

20 tests (P/N 09408592190)

2 **cobas**® transfer pipette packs (12 pipettes/pack - P/N 09329676001)

1 Package Insert Barcode card

Reagents in cobas® SARS-CoV-2 assay tube	Reagent ingredients	Safety symbol and warning[a]
cobas® Liat® Internal Process Control	Tris buffer, tween-80, polyethylene glycol, EDTA, < 0.001% stock bacteriophage MS2 (inactivated), 0.002% carrier RNA, 0.01% ProClin® 300 preservative	EUH210 Safety data sheet available on request. EUH208 Contains Mixture of: 5-chloro-2- methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1). May produce an allergic reaction.
Proteinase K	100% Proteinase K	N/A
cobas® Liat® Magnetic Glass Particles	Magnetic Glass Particles	N/A

Reagents in cobas® SARS-CoV-2 assay tube	Reagent ingredients	Safety symbol and warning[a]
cobas® Liat® Lysis Buffer	Citric acid, sodium phosphate, 42.6% guanidinium isothiocyanate[b], 5% decaethylene glycol monododecyl ether[b], dithiothreitol	 **DANGER** H302 + H332 Harmful if swallowed or if inhaled. 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. P261 Avoid breathing dust/fume/gas/mist/ vapours/spray. P273 Avoid release to the environment. P280 Wear protective gloves/protective clothing/ eye protection/face protection/hearing protection. 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 9002-92-0 Brij 35
cobas® Liat® Wash Buffer	Glycine, potassium fluoride, 0.01% ProClin® 300 preservative	N/A
cobas® Liat® Elution Buffer	Trehalose, tris buffer, magnesium sulfate, bovine serum albumin, 0.01% ProClin® 300 preservative	EUH210 Safety data sheet available on request. EUH208 Contains Mixture of: 5-chloro-2- methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1). May produce an allergic reaction.
cobas® Liat® SARS-CoV-2 Master Mix-1	Tween-80, tris buffer, trehalose, potassium chloride, bovine serum albumin, dATP, dCTP, dGTP, dUTP, 0.01% ProClin® 300 preservative, < 0.001% Downstream SARS-CoV-2 and Internal Process Control primers	EUH210 Safety data sheet available on request. EUH208 Contains Mixture of: 5-chloro-2- methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1). May produce an allergic reaction.
cobas® Liat® SARS-CoV-2 Master Mix-2	Tween-80, tween-20, tris buffer, glycerol, potassium chloride, EDTA, dithiothreitol, < 0.01% Z05 polymerase with aptamer, 0.23% MMLV Reverse Transcriptase	N/A
cobas® Liat® SARS-CoV-2 Master Mix-3	Tween-80, tris buffer, EDTA, trehalose, potassium chloride, bovine serum albumin, < 0.001% upstream SARS-CoV-2 and Internal Control primers, < 0.01% fluorescent-labeled SARS-CoV-2 and Internal Control probes, 0.004% Taq DSC 2.0 DNA polymerase, 0.01% ProClin® 300 preservative	EUH210 Safety data sheet available on request. EUH208 Contains Mixture of: 5-chloro-2- methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1). May produce an allergic reaction.

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

[b]Hazardous substance or mixture.

Table 2 **cobas**® SARS-CoV-2 Quality Control Kit

cobas® SARS-CoV-2 Quality Control Kit

Store at 2-8°C
(P/N 09408835190)

8 transfer pipettes

1 Control Kit Barcode card

Kit components	Reagent ingredients	Quantity per kit	Safety symbol and warning[a]
cobas® SARS-CoV-2 Positive Control **SARS-CoV-2 (+) C** (P/N 09212078001)	Tris buffer, EDTA, < 0.003% Poly rA (synthetic), < 0.01% non-infectious plasmid DNA (microbial) containing SARS-CoV-2 sequence, < 0.05% sodium azide	3 X 0.25 mL	N/A
cobas® Dilution UTM **Dilution UTM (-) C** (P/N 08053669001)	N/A	3 X 0.3 mL	N/A

[a] Product safety labeling primarily follows EU GHS guidance

Reagent storage and handling

Reagents shall be stored and will be handled as specified in Table 3.

Do not freeze materials listed below. Do not open individual assay tube packaging until operator is ready to perform testing.

Table 3 Reagent storage and handling

Reagent	Storage Temperature	Storage Time
cobas® SARS-CoV-2	2–8°C	Stable until the expiration date indicated on the label
cobas® SARS-CoV-2 Quality Control Kit	2-8°C	Stable until the expiration date indicated on the label

Additional materials required

Table 4 Materials required but not provided

Specimen Collection Kit	P/N
Nasopharyngeal Swab Collection Kits: Flexible minitip FLOQSwab™ with Universal Transport Media™ (UTM®) from Copan Diagnostics OR BD™ Universal Viral Transport (UVT) 3-mL collection kit with a flocked flexible minitip swab	305C, 307C, 321C, 3C057N, 3C071N 220529, 220531
Nasal Swab Collection Kits: Regular FLOQSwab™ with Universal Transport Media™ (UTM®) from Copan Diagnostics, OR BD™ Universal Viral Transport (UVT) 3-mL collection kit with a regular flocked swab, OR Copan Universal Transport Medium (UTM-RT®), without beads	306C, 321C, 346C, 3C064N 220527, 220528 3C047N, 3C075N

The following additional collection media for use with **cobas**® SARS-CoV-2 have been evaluated in analytical studies and may be acceptable. These media have not been evaluated in the clinical study.

Specimen Collection Media	P/N
Thermo Fisher™ Scientific Remel™ M4RT Thermo Fisher™ Scientific Remel™ M4 Thermo Fisher™ Scientific Remel™ M5 Thermo Fisher™ Scientific Remel™ M6 Thermo Fisher™ Scientific Remel™ M4RT® tube, without beads	R12565, R12566, R12567 R12550 R12555 R12563, R12568, R12569 R12622, R12591
Pre-aliquoted 3 mL 0.9% or 0.85% Physiological saline Thomas Scientific MANTACC™ 0.9% Saline Solution, 3 mL in 10 mL Tube, 50 Tubes per Pack, or equivalent Millennium LifeSciences, Inc. Culture Media Concepts®, 3 mL Sterile Normal Saline (0.85%) in 10 mL plastic tube (15 x 100 mm)	 20A00K984 V468-3

Instrumentation and software required

The **cobas**® Liat® System Software is installed on the instrument(s).

Table 5 Equipment and software required but not provided

Equipment and Software
cobas® Liat® Analyzer (P/N 07341920190) Including **cobas**® Liat® System Software (Core) Version 3.3 or higher
cobas® SARS CoV-2 Assay Script v1.1 or higher

Note: For additional information regarding the **cobas**® Liat® Analyzer, please refer to the **cobas**® Liat® System User Guide.

Precautions and handling requirements

Warnings and precautions

- For in vitro diagnostic use.
- CLIA Complexity: WAIVED
  A Certificate of Waiver is required to perform this test in a CLIA Waived setting. To obtain CLIA waiver information and a Certificate of Waiver, please contact your state health department. Additional CLIA waiver information is available at the Centers for Medicare and Medicaid website at www.cms.hhs.gov/CLIA. Failure to follow the instructions or modification to the test system instructions will result in the test no longer meeting the requirements for waived classification.
- Before using the **cobas**® SARS-CoV-2 test, operator should carefully read Instructions For Use (IFU) and the **cobas**® Liat® System User Guide.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Do not use a damaged **cobas**® SARS-CoV-2 assay tube.
- Do not use a **cobas**® SARS-CoV-2 assay tube that has been dropped after removal from its foil pouch.
- Do not open the cap of the **cobas**® SARS-CoV-2 assay tube during or after the run on the **cobas**® Liat® Analyzer.
- Do not use Negative Control if the color has changed from light orange-red.
- 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.
- For additional warnings, precautions and procedures to reduce the risk of contamination for the **cobas**® Liat® Analyzer, consult the **cobas**® Liat® System User Guide.
- Dispose of a used **cobas**® SARS-CoV-2 assay tube, pipette and specimen tube according to your institution's safety guidelines for hazardous material.
- On request Safety Data Sheets (SDS) are available from your local Roche representative.
- Due to the high sensitivity of the assays run on the **cobas**® Liat® Analyzer, contamination of the work area with previous positive samples may cause false positive results. Handle samples according to standard laboratory practices. Clean instruments and surrounding surfaces according to instructions provided in the cleaning section of the **cobas**® Liat® System User Guide. If spills occur on the **cobas**® Liat® Analyzer, follow the appropriate instructions in the **cobas**® Liat® System User Guide to clean.
- Specimen collection must be performed using the recommended swab types. Inadequate or inappropriate sample collection, storage, and transport may yield incorrect or invalid test results. DO NOT use cotton or calcium alginate swabs, or swabs with wood shafts.
- When using pre-aliquoted 3 mL of sterile 0.9% or 0.85% physiological saline solution, ensure that the swab height is appropriate for the collection and the score mark is not higher than the height of the collection tube.
- Ensure there is no sign of leakage from the collection tube prior to running the test.
- Use only transfer pipettes provided in either the **cobas**® Liat® Assay Kit or **cobas**® Liat® Quality Control Kit to transfer controls and samples into the assay tube. Use of alternative transfer pipettes may lead to invalid results.
- Good laboratory practices and careful adherence to the procedures specified in this Instructions For Use document are necessary. Wear laboratory gloves, laboratory coats, and eye protection when handling samples and reagents. Gloves must be changed when taking transfer pipette out of the **cobas**® transfer pipette pack, between handling samples, **cobas**® SARS-CoV-2 assay tube, and **cobas**® SARS-CoV-2 Quality Control Kit to avoid contamination of reagents and pipettes.

- After handling samples and kit reagents, remove gloves and wash hands thoroughly.

Sample collection, transport, and storage

Note: Handle all samples and controls as if they are capable of transmitting infectious agents. Do not use cotton or calcium alginate swab, or swab with wood shafts.

Sample collection

- Collect specimens using a sterile flocked swab with a synthetic tip according to applicable manufacturer instructions and/or standard collection technique using 3 mL of viral transport media or sterile 0.9% or 0.85% physiological saline.

Transport and storage

Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents. Transport and test specimens as soon as possible after collection.

- If transportation is required, specimens must be packaged, shipped, and transported according to the current edition of the International Air Transport Association (IATA) Dangerous Goods Regulation. Follow shipping regulations for UN 3373 Biological Substance, Category B when sending potential SARS-CoV-2 virus specimens. Store specimens at 2-8°C and ship overnight on ice pack. If a specimen is frozen at ≤-70°C, ship overnight on dry ice.
- Specimens transferred into the **cobas**® SARS-CoV-2 assay tube should be run as soon as possible on the Analyzer. Once the sample has been added to the **cobas**® SARS-CoV-2 assay tube it may be stored at room temperature for up to 4 hours.
- Specimens collected in transport media (UTM or UVT, M4, M4RT, M5 and M6) may be stored up to 4 hours at room temperature or up to 72 hours at 2-8°C if immediate testing is not possible. Freezing at -70°C or colder (and transportation on dry ice) is required for specimen storage or transportation beyond 72 hours prior to the specimen being added to the assay tube for testing.
- Specimens collected in 0.9% or 0.85% physiological saline solution may be stored up to 4 hours at room temperature or up to 72 hours at 2-8°C if immediate testing is not possible.
- The 0.9% physiological saline solution and Remel™ media (M4, M4RT, M5 and M6) are compatible for use with **cobas**® SARS-CoV-2 test. Performance of the **cobas**® SARS-CoV-2 test with specimens collected in 0.9% physiological saline and Remel™ media has been established in analytical studies, however, clinical performance of the assay in this media types was not established.

Instructions for use

Procedural notes

- Do not use **cobas**® SARS-CoV-2 assay tube and **cobas**® SARS-CoV-2 Quality Control Kit after their expiry dates.
- Do not reuse assay tubes and transfer pipettes. They are for one-time use only.
- Refer to the **cobas**® Liat® System User Guide for detailed operation and routine cleaning of instruments.

Running cobas® SARS-CoV-2

Use the transfer pipette to load approximately 0.2 mL of the specimen into the **cobas**® SARS-CoV-2 assay tube. The **cobas**® Liat® Analyzer will adjust the sample volume if more sample was loaded.

Always use caution when transferring specimens from a sample collection tube to the assay tube.

Use transfer pipettes from the cobas® transfer pipette pack included in the kit to handle specimens.

Ensure clean gloves are used when removing transfer pipettes from the cobas® transfer pipette pack.

Reseal the cobas® transfer pipette pack immediately after removing the necessary pipette(s).

The cobas® transfer pipette pack may be stored at room temperature following first removal from the kit.

Always use a new transfer pipette for each specimen.

The test procedure is described in detail in the **cobas**® Liat® System User Guide. Figure 1 below summarizes the procedure.

Test procedure

Figure 1 cobas® SARS-CoV-2 procedure

"Lot Validation" workflow

1	Start up the system and login
2	Obtain Controls and assay tubes
3	Under "Assay Menu", choose "New Lot"
4	Scan the Package Insert barcode from the Package Insert Barcode card
5	Scan and run Negative Control
6	Scan and run Positive Control

cobas® SARS CoV-2 workflow

1	Start up the system and login
2	Obtain samples and assay tubes
3	On the Main menu, choose "Run Assay"
4	Scan the **cobas**® SARS-CoV-2 assay tube barcode
5	Scan or enter the sample ID
6	Add specimen to the **cobas**® SARS-CoV-2 assay tube using the transfer pipette and re-cap the tube
7	Re-scan the **cobas**® SARS-CoV-2 assay tube barcode
8	Start run
9	Review results*
10	Unload and dispose of the used **cobas**® SARS-CoV-2 assay tube

*Refer to **cobas**® Liat® System User Guide for details of result uploading to LIS or DMS.

cobas® SARS-CoV-2 assay tube Lot Validation

Before using a new lot of **cobas**® SARS-CoV-2 assay tubes, a Lot Validation procedure must be performed on the **cobas**® Liat® Analyzer to validate the **cobas**® SARS-CoV-2 assay tube lot at your site. The procedure includes running a Negative Control sample and a Positive Control sample.

Note: Refer to the **cobas**® Liat® System User Guide for detailed operating instructions.

Materials needed for Lot Validation

The following materials are needed:

Materials needed to validate Negative Control:	Materials needed to validate Positive Control:
□ 1 Dilution UTM tube[2] □ 1 **cobas**® SARS-CoV-2 assay tube from this lot[1] □ 1 transfer pipette[1 or 2] □ Package Insert Barcode card[1] □ Negative Control barcode on the Control Kit Barcode card[2]	□ 1 **cobas**® SARS-CoV-2 Positive Control Vial[2] □ 1 **cobas**® SARS-CoV-2 assay tube from this lot[1] □ 1 transfer pipette[1 or 2] □ Positive Control barcode on the Control Kit Barcode card[2]

[1]Contained in **cobas**® SARS-CoV-2 assay tube Kit

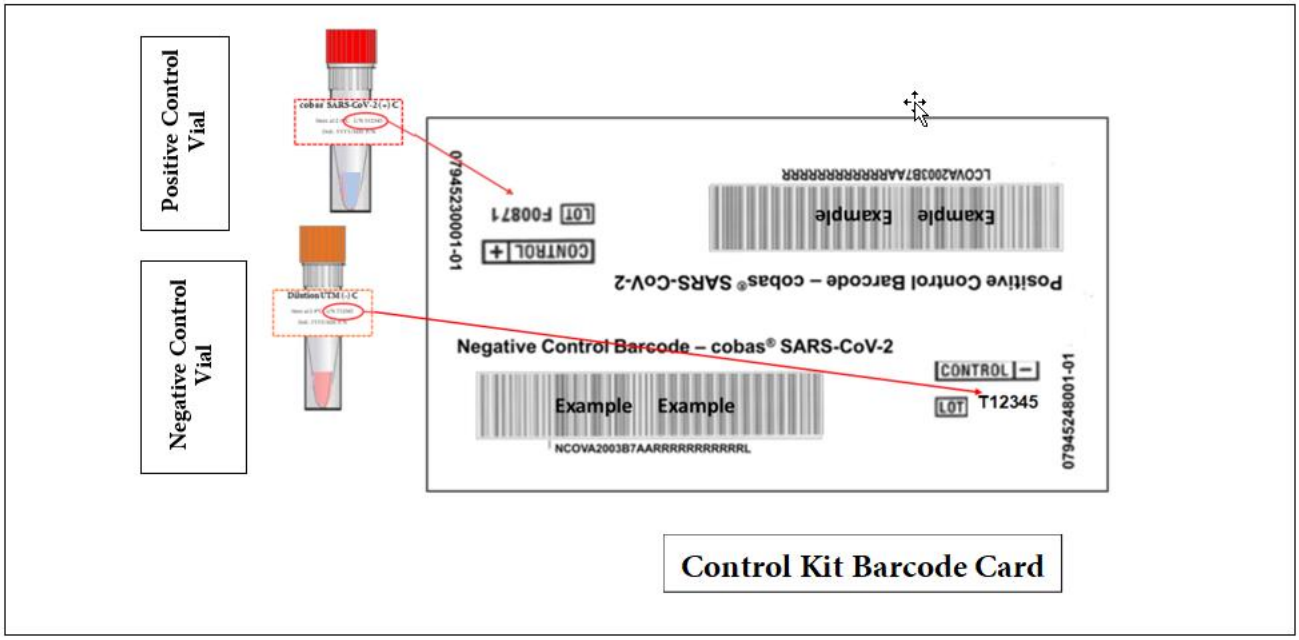
- Package Insert Barcode card: This barcode is lot-specific; match the lot number next to the barcode with the lot number on the **cobas**® SARS-CoV-2 assay tubes.

[2]Contained in **cobas**® SARS-CoV-2 Quality Control Kit

Note: Following Figure 2:

- Match the lot number (L/N) of the Dilution UTM tube label to the lot number (LOT) of the Negative Control barcode on the Control Kit Barcode card and then use the Negative Control barcode (on the Control Kit Barcode card) as the sample ID when performing a negative control run.
- Match the lot number (L/N) of the Positive Control Vial label for **cobas**® SARS-CoV-2 to the lot number (LOT) of the Positive Control barcode on the Control Kit Barcode card as shown in Figure 2. Use the Positive Control barcode (on the Control Kit Barcode card) as the sample ID when performing a positive control run.

Figure 2 Schematic diagram for illustrating Negative Control Vial, Positive Control Vial and Control Kit Barcode Card



Assay tube Lot Validation workflow

1. Press the power on/off button to start the **cobas**® Liat® Analyzer.
2. Choose **"Login"** on the screen of the **cobas**® Liat® Analyzer.
3. Enter user name when prompted, choose "**OK**".
4. Enter user password when prompted, choose "**OK**".

   Note: You may be prompted to confirm you have read the User Manual, (i.e., cobas® Liat® System User Guide).
5. From the Main menu, choose "**Assay Menu**".
6. Choose "**New Lot**" at the bottom of the list.
7. When prompted to **Scan insert ID,** choose "**Scan**" and scan the **cobas**® SARS-CoV-2 Package Insert barcode from the Package Insert Barcode card. Ensure that the red scan light is over the entire barcode.

   Note: You may be prompted to confirm you have read Instructions For Use.
8. When prompted to **Scan negative control ID**, choose "**Scan**" and scan the Negative Control barcode from the Control Kit Barcode card included with the control kit. Ensure that the red scan light is over the entire barcode. Next, the **cobas**® Liat® Analyzer will prompt with the message "**Add negative control & scan tube ID**".
9. Hold a tube of Negative Control upright and lightly tap on a flat surface to collect liquid at the bottom of the tube. Visually check that the Dilution UTM has pooled at the bottom of the tube.
10. Open up a **cobas**® SARS-CoV-2 assay tube foil pouch (from the lot to be added) and remove the contents.

11. Use a transfer pipette provided in the kit to add the Negative Control to the **cobas**® SARS-CoV-2 assay tube. Firmly squeeze the bulb of the pipette until the bulb is fully flat, then insert the tip of the pipette into the liquid and draw up the sample by slowly releasing the bulb.

    Note: Only use transfer pipettes provided in either the cobas® Liat® Assay Kit or cobas® Liat® Quality Control Kit to transfer controls and samples into the assay tube.

12. Carefully remove the cap of the **cobas**® SARS-CoV-2 assay tube and insert the pipette into the opening. Place the pipette tip near the bottom of the open segment.

13. Slowly squeeze the bulb to empty the contents of the pipette into the **cobas**® SARS-CoV-2 assay tube. Avoid creating bubbles in the sample. Do not release the pipette bulb while the pipette is still in the **cobas**® SARS-CoV-2 assay tube.

    Note: Do not puncture the cobas® SARS-CoV-2 assay tube or the seal at the bottom of the sample compartment. If either of these are damaged, discard both the cobas® SARS-CoV-2 assay tube and the transfer pipette, and restart the testing procedure with a new cobas® SARS-CoV-2 assay tube and pipette.

14. Screw the cap back onto the **cobas**® SARS-CoV-2 assay tube. Dispose of the transfer pipette as biohazardous material.

15. Choose "**Scan**" and place the **cobas**® SARS-CoV-2 assay tube horizontally on the table beneath the barcode reader so that the red scan light is over the entire barcode. The tube entry door on top of the **cobas**® Liat® Analyzer will open automatically once the barcode is read.

16. Remove the **cobas**® SARS-CoV-2 assay tube sleeve and immediately insert the **cobas**® SARS-CoV-2 assay tube into the **cobas**® Liat® Analyzer until the tube clicks into place.

    Note: The cobas® SARS-CoV-2 assay tube only fits in one way - the grooved side of the cobas® SARS-CoV-2 assay tube must be on the left while the cap is on top.

17. If the tube is not inserted by the time the door closes, re-scan the **cobas**® SARS-CoV-2 assay tube barcode and insert the **cobas**® SARS-CoV-2 assay tube again. Once the **cobas**® SARS-CoV-2 assay tube is properly inserted, the **cobas**® Liat® Analyzer will close the door automatically and begin the test.

18. During the test, the **cobas**® Liat® Analyzer displays the running status and estimated time remaining. Once the test is complete, the **cobas**® Liat® displays the message, "*Remove the assay tube slowly and carefully.*" and opens the tube entry door automatically. Slowly lift the **cobas**® SARS-CoV-2 assay tube out of the **cobas**® Liat® Analyzer. Dispose of the used **cobas**® SARS-CoV-2 assay tube as biohazardous material.

19. If **"Negative control result accepted."** is displayed at the end of the run, choose **"Confirm"**. If the result is rejected, repeat the negative control run (steps 8-19). If repeated control runs do not produce the expected results, contact your local Roche representative.

20. Choose **"Back"** to proceed with the **cobas**® SARS-CoV-2 Positive Control test on the same instrument.

21. Similarly, follow steps 8 to 18 with a **cobas**® SARS-CoV-2 Positive Control in place of the **cobas**® Liat® Negative Control.

22. If "**Positive control result accepted. Lot … added**" is displayed at the end of the run, choose "**Confirm**" and then choose "**Back**" to return to Main menu. If the result is rejected, repeat the **cobas**® Liat® SARS-CoV-2 Positive Control test. If repeated control runs do not produce the expected results, contact your local Roche representative.

23. Choose "**Assay Menu"** to verify the new lot has been added.

Transferring assay tube lot information

After Lot Validation workflow is completed on one Analyzer, use the Advanced Tools to transfer the lot information to the other Analyzers at your site. This allows the other Analyzers to use this **cobas**® SARS-CoV-2 assay tube lot without performing Lot Validation on each Analyzer. Consult the **cobas**® Liat® System User Guide for details of operation.

cobas® SARS-CoV-2 on clinical specimens testing

Material needed for running cobas® SARS-CoV-2

- **cobas**® SARS-CoV-2 assay foil pouch which includes the **cobas**® SARS-CoV-2 assay tube
- 1 transfer pipette
- 1 specimen in collection media

Procedure

1. Ensure that the **cobas**® Liat® Analyzer is powered on.
2. Choose **"Login"** on the screen of the **cobas**® Liat® Analyzer.
3. Enter user name when prompted, choose **"OK"**.
4. Enter user password when prompted, choose **"OK"**.

   Note: You may be prompted to confirm you have read the User Manual (i.e., cobas® Liat® System User Guide).
5. From the Main menu, choose "**Run Assay**".
6. Open up a **cobas**® SARS-CoV-2 assay tube pouch and take out the assay tube. When prompted to **Scan tube ID**, choose **"Scan"** and place the SARS-CoV-2 assay tube horizontally on the table beneath the barcode reader so that the red scan light is over the entire barcode.
7. When prompted to **Scan sample ID**, choose "**Scan**" to scan the sample barcode. In the case that the sample cannot be scanned, choose "**Enter**" to manually enter the sample ID.
    a. **Note:** If patient verification is activated, the Analyzer will display the status of verification.
        i. If patient verification is successful, the Analyzer may prompt confirmation of entered information before proceeding with running the assay.
        ii. If patient verification fails, the Analyzer may display a notification that verification failed:
            1. And may require acknowledgement before proceeding with running the assay or
            2. If unable to proceed with running the assay, contact your lab administrator.
8. Carefully remove one transfer pipette from the **cobas**® transfer pipette pack and avoid touching other pipettes in the pack. Re-seal the pack.
9. When prompted to **add the sample,** use the transfer pipette provided in the assay kit to transfer specimen. Firmly squeeze the bulb of the pipette until the bulb is fully flat, then insert the tip of the pipette into the liquid and draw up the sample by slowly releasing the bulb.

10. Carefully remove the cap of the **cobas**® SARS-CoV-2 assay tube and insert the pipette into the opening. Place the pipette tip near the bottom of the open segment.
11. Slowly squeeze the bulb to empty the contents of the pipette into the **cobas**® SARS-CoV-2 assay tube. Do not release the pipette bulb while the pipette is still in the **cobas**® SARS-CoV-2 assay tube.

    Note: Do not puncture the cobas® SARS-CoV-2 assay tube or the seal at the bottom of the sample compartment. If either of these are damaged, discard both the cobas® SARS-CoV-2 assay tube and the transfer pipette, and restart the testing procedure with a new cobas® SARS-CoV-2 assay tube and pipette.

12. Re-cap the **cobas**® SARS-CoV-2 assay tube and dispose of the transfer pipette as biohazardous material.

    Note: Avoid contaminating gloves, equipment and work surfaces with the residual contents of the pipette.

13. Choose "**Scan"** and rescan the same **cobas**® SARS-CoV-2 assay tube barcode. The tube entry door on top of the **cobas**® Liat® Analyzer will open automatically.
14. Remove the **cobas**® SARS-CoV-2 assay tube sleeve and immediately insert the **cobas**® SARS-CoV-2 assay tube into the **cobas**® Liat® Analyzer until the tube clicks into place.

    Note: The SARS-CoV-2 assay tube only fits in one way - the grooved side of the cobas® SARS-CoV-2 assay tube must be on the left while the cap is on top.

15. If the assay tube is not inserted by the time the door closes, re-scan the **cobas**® SARS-CoV-2 assay tube barcode and insert the **cobas**® SARS-CoV-2 assay tube again. Once the **cobas**® SARS-CoV-2 assay tube is properly inserted, the **cobas**® Liat® Analyzer will close the door automatically and begin the test.
16. During the test, the **cobas**® Liat® Analyzer displays the running status and estimated time remaining. Once the test is complete, the **cobas**® Liat® Analyzer displays the message, "*Remove the assay tube slowly and carefully."* and opens the tube entry door automatically. Slowly lift the **cobas**® SARS-CoV-2 assay tube out of the **cobas**® Liat® Analyzer. Dispose of the used **cobas**® SARS-CoV-2 assay tube as biohazardous material.
17. Choose "**Report"** to see the Result Report. If applicable, choose "**Print"** to print the report.
18. Choose "**Back"**, and then "**Main"** to return to the Main menu to perform the next test.

Performing additional control runs

In accordance with local, state, federal and/or accrediting organization requirements, additional control runs may be performed with a lot of **cobas**® SARS-CoV-2 assay tubes that has already been added through the "Lot Validation" workflow. Use the **cobas**® SARS-CoV-2 Quality Control Kit for use on the **cobas**® Liat® System to conduct these runs.

Materials needed for additional control runs

- **cobas**® SARS-CoV-2 assay tubes
- Transfer pipette(s)
- **cobas**® Liat® SARS-CoV-2 Positive Control and/or Negative Control
- Corresponding barcodes for the **cobas**® SARS-CoV-2 Positive Control and/or the Negative Control

Procedure

Use the procedure outlined under the section "**cobas**® SARS-CoV-2 on clinical specimens testing" to perform additional control runs. In step **7**, be sure to use the provided control barcodes included in **cobas**® SARS-CoV-2 Control Kit to scan as sample ID barcodes. Interpretation of results for **cobas**® SARS-CoV-2 when running additional **cobas**® SARS-CoV-2 Positive Controls or Negative Controls are shown in the "Interpretation of results" section (Table 6 through Table 8). Using barcodes other than the control barcodes provided may lead to incorrect control results.

Results

Quality control and interpretation of results

Table 6 Interpretation of results of **cobas**® SARS-CoV-2 when running "Lot Validation" procedure

cobas® Liat® Analyzer Display	Interpretation
Negative Control Valid	**Negative Control Valid** Control is negative for the presence of SARS-CoV-2 RNA.
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 SARS-CoV-2 RNA.
Positive Control Invalid. Repeat Run	**Positive Control Invalid** Result is Invalid. The Positive Control should be re-tested to obtain valid result. Repeat Run.

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

Table 7 Interpretation of results of **cobas**® SARS-CoV-2 when running a sample

Result Report	Interpretation
SARS-CoV-2: SARS-CoV-2 Not Detected	Negative test for SARS-CoV-2 (no SARS-CoV-2 RNA detected)
SARS-CoV-2: SARS-CoV-2 Detected	Positive test for SARS-CoV-2 (SARS-CoV-2 RNA present)
Assay Invalid	Presence or absence of SARS-CoV-2 cannot be determined. Repeat assay with same sample or, if possible, collect new sample for testing.
Assay Aborted by System	Run failed or aborted by system. Repeat assay with same sample or, if possible, collect new sample for testing.
Assay aborted by script: Script aborted	Run failed or aborted by script. Repeat assay with same sample or, if possible, collect new sample for testing.
Assay Aborted by User	Run aborted by user.

Table 8 Interpretation of results when running additional controls after following "Lot Validation" procedure

Positive control

cobas® Liat® Analyzer Display	Interpretation
Positive Control Valid	**Positive Control Valid** Control is positive for the presence of SARS-CoV-2 RNA.
Positive Control Invalid	**Positive Control Invalid** Result is Invalid. The Positive Control should be re-tested to obtain valid result. Repeat Run.

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

Negative control

cobas® Liat® Analyzer Display	Interpretation
Negative Control Valid	**Negative Control Valid** Control is negative for the presence of SARS-CoV-2 RNA.
Negative Control Invalid	**Negative Control Invalid** Result is Invalid. The Negative Control should be re-tested to obtain valid result. Repeat Run.

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

Procedural limitations

- For prescription use only.
- **cobas**® SARS-CoV-2 test has been evaluated only for use in combination with the **cobas**® SARS-CoV-2 Quality Control Kit and this Instructions For Use document. Modifications to these procedures may alter the performance of the test.
- Due to inherent differences between technologies, it is recommended that, prior to switching from one technology to the next, users perform method correlation studies in their laboratory to qualify technology differences. One hundred percent agreement between the results should not be expected due to aforementioned differences between technologies. Users should follow their own specific policies/procedures.
- This test is intended to be used for the detection of SARS-CoV-2 RNA in nasopharyngeal and nasal swab samples collected in a Copan UTM System (UTM) or BD™ Universal Viral Transport System (UVT) or Thermo Fisher™ Scientific Remel™ media, Thomas Scientific MANTACC™ premeasured 3 mL 0.9% physiological saline solution or Millennium LifeSciences, Inc. Culture Media Concepts® 3mL Sterile Normal Saline (0.85%). Testing of other sample or media types may lead to inaccurate results.
- Performance of the cobas® SARS-CoV-2 test with specimens collected in 0.9% physiological saline and Remel™ media (M4RT, M5, M6, M4) are compatible, however, they have been evaluated in analytical studies only, and the clinical performance with these media has not been evaluated.
- Users in a point of care environment should not prepare (formulate, measure, aliquot) 0.9% or 0.85% physiological saline. CLIA certified moderate and high complexity laboratories may prepare and package equivalent 3 mL of physiological saline for use with **cobas**® SARS-CoV-2 test, but performance with these alternative solutions has not been established. When using a physiological saline solution, ensure that the collection tube is an appropriate height for the swab such that the score mark on the swab is not higher than the height of the tube.
- As with other tests, negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for treatment or other patient management decisions.
- A negative test result does not preclude the possibility of infection with other bacteria or viruses.
- Detection of SARS-CoV-2 RNA may be affected by sample collection methods, patient factors (e.g., presence of symptoms), and/or stage of infection.
- False negative results may occur if a specimen is improperly collected, transported or handled, if there is insufficient RNA to be detected, or if one or more target viruses inhibits amplification of other targets.
- 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.
- Mutations within the target regions of **cobas**® SARS-CoV-2 could affect primer and/or probe binding that results in failure to detect the presence of virus.
- Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the common variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.
- False negative or invalid results may occur due to interference. The Internal Control is included in **cobas**® SARS-CoV-2 to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- For asymptomatic individuals with negative results, results should be considered presumptive. Additionally, a negative result obtained with a nasal swab collected from an asymptomatic patient should be followed up by testing at least twice over three days with at least 48 hours between tests.

- The clinical performance characteristics of this device were established during the 2021-2022 SARS-CoV-2 pandemic, when the Alpha, Delta, and Omicron variants were prevalent; due to the propensity of the virus to mutate, new strains emerge over time which may affect the performance of this device and may have serious public health implications. Additional testing with a molecular test and/or sequencing should be considered in situations where a new virus strain or variant is suspected.

Expected values

The SARS-CoV-2 positivity rate observed during the clinical study, as determined by the **cobas**® SARS CoV-2 test, is presented by enrollment site in Table 9.

Table 9 Positivity rate for SARS-CoV-2 (as determined by **cobas**® SARS-CoV-2).

Clinical Site ID	Site Location	NPS Specimens Total No.	NPS Specimens No. Positive for SARS- CoV-2	NPS Specimens Positivity (%) (Expected value)	NS Specimens Total No.	NS Specimens No. Positive for SARS- CoV-2	NS Specimens Positivity (%) (Expected value)
-	Overall	1828	162	8.9%	1826	153	8.4%
1	Albuquerque, NM	222	2	0.9%	222	0	0.0%
2	Vienna, VA	390	60	15.4%	390	61	15.6%
3	Northridge, CA	97	0	0.0%	96	0	0.0%
4	Savannah, GA	385	20	5.2%	384	18	4.7%
5	North Miami, FL	343	23	6.7%	342	18	5.3%
6	Indianapolis, IN	9	1	11.1%	8	1	12.5%
7	Las Vegas, NV	105	1	1.0%	105	1	1.0%
8	Evanston, IL	131	34	26.0%	131	32	24.4%
9	Seneca, SC	30	1	3.3%	33	2	6.1%
10	Rochester, NY	116	20	17.2%	115	20	17.4%

Non-clinical performance – SARS-CoV-2

Analytical sensitivity

Limit of detection (LoD) studies determine the lowest detectable concentration of SARS-CoV-2 at which greater or equal to 95% of all (true positive) replicates test positive.

SARS-CoV-2 viral culture

To determine the LoD for SARS-CoV-2, a heat inactivated cultured virus of an isolate from a US patient (USA-WA1/2020, lot number 324047, ZeptoMetrix, NY, USA) was serially diluted in pooled negative nasopharyngeal swab matrix. Five concentration levels were tested with 20 replicates except for the highest concentration level, which was tested with 10 replicates. Three lots of assay tubes (approximately equal numbers of replicates per lot) and two independent dilution series (equal numbers of replicates per dilution series) were used in the study.

As shown in Table 10, the lowest concentration level with observed hit rates greater than or equal to 95% was 0.012 $TCID_{50}$/mL (12 copies/mL) for SARS-CoV-2.

Table 10 LoD determination using USA-WA1/2020 strain

Strain – USA-WA1/2020 (stock concentration 3.16E+06 $TCID_{50}$/mL)

Concentration [$TCID_{50}$/mL]	Concentration [copies/mL]*	Total valid results	Hit rate [%]	Mean Ct**
0.048	49	10	100	33.0
0.024	24	20	100	33.6
0.012	12	20	95	34.7
0.006	6	20	90	35.4
0.003	3	20	55	35.5

*Concentration of each viral stock in copies/mL was quantified using Reverse transcriptase digital PCR with target specific PCR primers and probe sets designed to amplify SARS-CoV-2.

**Calculations only include positive results.

WHO International Standard

The LoD using WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146) was determined by reconstituting the WHO Standard to 0.5 mL according to the WHO NIBSC code: 20/146 Instructions for use (Version 1.0, Dated 14/12/2020). Following reconstitution, the WHO Standard was diluted to an intermediate stock (IS) concentration in UTM.

WHO Standard IS was serially diluted in pooled negative clinical nasopharyngeal swabs matrix. Six concentration levels were tested with 24 replicates at each level across three lots of assay tubes (8 replicates per lot). Three independent dilution series were used in the study with approximately equal numbers of replicates per dilution series. The LoD was determined to be 30 IU/mL.

The results of the LoD study are shown in Table 11 below.

Table 11 Hit rate and mean Ct results of SARS-CoV-2 LoD determination

Strain – WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146)

Concentration [IU/mL]	Valid Positive Results	Total Valid Results	Hit Rate [%]	Mean Ct*
120	24	24	100	32.74
60	24	24	100	33.81
30	24	24	100	34.28
20	21	24	88	34.97
15	19	24	79	35.48
7.5	9	24	38	36.05

*Calculations only include positive results

Reactivity/inclusivity

The inclusivity study evaluates the assay ability to detect SARS-CoV-2 isolates/variants. In this study, sixteen (16) SARS-CoV-2 isolates/variants were tested. The isolates/variants were tested as inactivated viruses diluted into pooled clinical negative nasopharyngeal swab matrices. The isolates/variants tested in the study and the concentrations that they can be detected at 100%, i.e., in 3 out of 3 replicates are listed in Table 12. In silico analysis of the oligo sets for SARS-CoV-2 (taxonomy ID 2697049) have been continuously performed since the onset of the pandemic and cobas SARS-CoV-2 test will detect all analyzed SARS-CoV-2 sequences in the GISAID (>14 M) database (as of 15th November, 2023).

Table 12 Summary of SARS-CoV-2 Inclusivity Testing

Isolate/Variant	Pango Lineage	WHO Label	Lowest Concentration Detected (cp/mL)
Italy-INMI1	not listed	N/A	5.0E+00
Hong Kong/VM20001061/2020	A	N/A	2.0E+01
UK variant	B.1.1.7	Alpha	5.0E+00
South Africa Variant	B.1.351	Beta	2.0E+01
USA/COR-22-063113/2022	BA5.5	Omicron	6.0E+00
USA/GA-EHC-2811C/2021	BA.1	Omicron	1.5E+00
hCoV-19/USA/MD-HP40900/2022	B.1.1.529, XBB.1.5	Omicron	6.0E+00
hCoV-19/USA/MD-HP38861/2022	B.1.1.529, BQ.1.1	Omicron	1.2E+01
hCoV-19/USA/MD-HP38288/2022	B.1.1.529, BF.7	Omicron	1.2E+01
hCoV-19/USA/MD-HP30386/2022	B.1.1.529, BA.4	Omicron	6.0E+00
USA/MD-HP24556/2022	BA.2.3	Omicron	1.2E+01
USA/MD-HP20874/2021	B.1.1.529	Omicron	6.0E+00
USA/CA-Stanford-15_S02/2021	B.1.617.1	Kappa	1.2E+01
USA/NY-Wadsworth-21025952/2021	B.1.526	Iota	1.2E+01
USA/PHC658/2021	B.1.617.2	Delta	3.6E+01
Japan/TY7-503/2021 (Brazil P.1)	P.1	Gamma	3.6E+01

Cross reactivity and Microbial Interference

Cross-reactivity and microbial interference of **cobas**® SARS-CoV-2 were evaluated by testing a panel of multiple unique sub-species of microorganisms. High titer stocks of the potentially cross-reacting microorganisms were spiked into pooled negative nasopharyngeal swab clinical matrix and tested for cross-reactivity with **cobas**® SARS-CoV-2, and into pooled negative nasopharyngeal swab clinical matrix spiked with 3x LoD concentrations of SARS-CoV-2 and tested for microbial interference. The testing concentrations for potentially interfering microorganisms are ≥1.0E+05 units/mL for viruses and ≥1.0E+06 units/mL for other microorganisms unless otherwise noted (Table 13).

None of the organisms tested interfered with **cobas**® SARS-CoV-2 performance.

Results show that the presence of the microorganisms at the concentrations tested did not interfere with the detection of SARS-CoV-2 by generating false negative results. Note that in presence of SARS-coronavirus (SARS-CoV-1) at 1e5 pfu/mL, 3x LoD concentrations of SARS-CoV-2 was not detected, when SARS-CoV-1 was at 1e4 pfu/mL, 3x LoD of SARS-CoV-2 can be detected indicating SARS CoV-1 at 1e5 pfu/mL or higher may interfere with SARS-CoV-2 detection. However, the likelihood of a co-infection with SARS CoV-1 is remote as the last confirmed case of SARS-CoV-1 was reported in 2004.

Table 13 Summary Cross-reactivity/Microbial Interference: list of organisms tested

Description	Concentration Tested*	Description	Concentration Tested*
Human coronavirus 229E	2.80E+05	*Aspergillus Flavus var. flavus*	1.00E+06
Human Coronavirus HKU1	1.38E+07	*Bordetella parapertussis*	1.00E+06
Human coronavirus OC43	3.16E+05	*Bordetella pertussis*	1.74E+06
Human Coronavirus, NL63	1.38E+06	*Candida albicans*	1.58E+07
SARS Coronavirus**	1.00E+05	*Chlamydia pneumoniae*	6.88E+06
SARS Coronavirus**	1.00E+04	*Corynebacterium flavescens*	1.00E+06
MERS Coronavirus	1.50E+07	*Escherichia coli*	1.00E+06
Adenovirus	2.88E+05	*Fusobacterium necrophorum subsp. necrophprum*	1.00E+06
Cytomegalovirus	1.00E+05	*Haemophilus influenzae*	2.00E+06
Enterovirus Type 71	1.05E+05	*Lactobacillus crispatus*	1.00E+06
Epstein-Barr virus	1.00E+05	*Legionella pneumophila*	1.38E+08
Human Metapneumovirus (hMPV)	1.60E+05	*Moraxella catarrhalis*	1.00E+06
Influenza A (Brisbane 59/07) H1N1	1.00E+05	*Mycobacterium tuberculosis*	5.75E+06
Influenza A (Kansas-14/2017)	1.99E+07	*Mycoplasma genitalium*	1.00E+06
Influenza B (Colorado-06/2017)	6.10E+08	*Mycoplasma pneumoniae*	3.45E+06
Influenza B (Florida/04/06)	1.00E+05	Nasal Wash	1:10
Measles	1.00E+05	*Neisseria flava*	1.00E+06
Mumps	1.00E+05	*Neisseria meningitidis*	1.00E+06
Parainfluenza Virus (hPIV)	1.60E+05	*Pneumocystis jirovecii*	1.59E+07
Parainfluenza Virus Type 1	1.26E+05	*Pneumocystis jirovecii* (Clinical sample)	1:10
Parainfluenza Virus Type 3	3.45E+05	*Pseudomonas aeruginosa*	2.03E+07
Parainfluenza Virus Type 4A	2.88E+05	*Staphylococcus aureus*	1.00E+06
Respiratory Syncytial Virus Type A	1.26E+05	*Staphylococcus epidermis*	1.20E+07
Rhinovirus	5.50E+05	*Streptococcus pneumoniae*	1.22E+06

Description	Concentration Tested*	Description	Concentration Tested*
-	-	*Streptococcus pyogenes*	6.25E+06
-	-	*Streptococcus salivarius*	6.63E+06

* TCID50/mL, EID50/mL, cp/mL PFU/mL, genome equiv/mL for viruses; CFU/mL, IFU/mL for bacteria and fungi.

** SARS CoV-1 at 1e5 pfu/mL or higher may interfere with SARS-CoV-2 detection. It did not interfere with the SARS-CoV-2 detection at 1e4 pfu/mL.

Endogenous and Exogenous Interference

Potentially interfering substances that may be commonly encountered in respiratory specimens were evaluated. Medically and/or physiologically relevant concentrations of potential interferents were tested with **cobas**® SARS-CoV-2. Each substance was tested, by introducing potential interferents into pooled negative nasopharyngeal swab specimens (NNPS) in UTM and tested with and without 3x LOD of SARS-CoV-2 target. As shown in Table 14 substances at the concentrations tested did not interfere in the detection of SARS-CoV-2.

Table 14 Endogenous and Exogenous Interference

Potential Interferent	Active Ingredient	Concentration Tolerated
Mucin	Purified mucin protein	5 mg/mL
Human Whole Blood	-	5% (v/v)
Peripheral blood mononuclear cell (PBMC)	-	1.0E+06 cells/mL
Nasal spray - Afrin / Anefrin	Oxymetazoline	5% (v/v)
Nasal corticosteroids - Flonase	Fluticasone	5% (v/v)
Nasal gel - Zicam	Galphimia glauca, Histaminum hydrochloricum, Luffa operculata, Sulphur	5% (v/v)
Throat lozenges, oral anesthetic and analgesic - Cepacol	Benzocaine, Menthol	5 mg/mL
Antibiotic, nasal ointment - Bactroban	Mupirocin	5 mg/mL
Antiviral drug - Relenza	Zanamivir	5 mg/mL
Antiviral drug - Tamiflu	Oseltamivir	7.5 mg/mL
Antimicrobial, systemic	Tobramycin	4 µg/mL
Influenza vaccine - FluMist	Live Quadrivalent 2022-2023 A/Victoria/1/2020 (H1N1) (an A/Victoria/2570/2019 (H1N1) pdm09 - like virus), A/Norway/16606/2021 (H3N2) (an A/Darwin/9/2021 (H3N2) - like virus), B/Phuket/3073/2013 (B/Yamagata lineage), and B/Austria/1359417/2021 (B/Victoria lineage) lineage)	5.93E+06 FFU/mL

Reproducibility

Reproducibility study assesses the total variability of the assay in detecting SARS-CoV-2 across operators, study sites, testing days, Analyzers, and assay tube lots. The reproducibility was evaluated at 3 study sites representative of CLIA-waived intended use settings. Two operators at each of the 3 sites tested a 3-member reproducibility panel in triplicate on 5 different days, for a total of ~270 runs (3 panel members x 3 replicates x 2 operators x 5 days x 3 sites). Nine Analyzers and 3 assay tube lots were used. The reproducibility panel comprises a low positive and a moderate positive for SARS-CoV-2, in addition to a negative sample. The expected result for the true negative panel member is "Not Detected," while the expected result for the low positive and moderate positive panel member is "Detected." Percent agreement with expected result, mean Ct, Ct SD, and Ct %CV are shown in Table 15.

Table 15 SARS-CoV-2 reproducibility

Panel Member	Total number of valid test runs	Site 1	Site 2	Site 3	All sites	All sites
-	-	Agreement with Expected Results	Agreement with Expected Results	Agreement with Expected Results	Avg. Ct ± SD (%CV)	Agreement (n/N) and (95% CI)
Negative	268	100.0% (90/90)	100.0% (88/88)	98.9% (89/90)	-	99.6% (267/268) (97.9%-99.9%)
SARS-CoV-2 Low Positive	266	100.0% (89/89)	100.0% (90/90)	97.7% (85/87)	33.4±0.96 (2.9%)	99.2% (264/266) (97.3%-99.8%)
SARS-CoV-2 Moderate Positive	268	100.0% (88/88)	100.0% (90/90)	100.0% (90/90)	32.5±0.54 (1.7%)	100.0% (268/268) (98.6%-100.0%)

Clinical performance evaluation

The clinical performance of the **cobas**® SARS-CoV-2 test was evaluated using prospectively collected fresh paired clinical nasopharyngeal swab (NPS) and nasal swab (NS) specimens and unpaired frozen specimens collected from either symptomatic individuals suspected of respiratory viral infection consistent with COVID-19 or asymptomatic individuals. Testing of clinical samples was performed with the **cobas**® SARS-CoV-2 test at 10 point-of-care healthcare facilities (e.g., emergency rooms, outpatient clinics, and physician offices). Results from clinical specimens tested with **cobas**® SARS-CoV-2 were compared to results from three highly sensitive FDA-EUA-authorized laboratory-based RT-PCR assays (composite comparator method).

Prospective clinical specimens were tested February–June 2022. In total, 1874 evaluable NPS samples and 1872 evaluable NS samples were included in the analysis for the performance evaluation of the **cobas**® SARS-CoV-2 assay. Of these, 673 NPS specimens were collected from individuals with signs and symptoms of respiratory tract infection and 1201 were from asymptomatic individuals (413 suspected of SARS-CoV-2 infection due to recent exposure or other reasons and 788 from individuals without symptoms or other reasons to suspect COVID-19). Among the NS specimens tested in the study, 674 were collected from individuals with signs and symptoms of respiratory tract infection and 1198 were from asymptomatic individuals (411 suspected of SARS-CoV-2 infection due to recent exposure or other reasons and 787 from individuals without symptoms or other reasons to suspect COVID-19).

For each specimen type (NPS and NS), 23 each frozen SARS-CoV-2-positive and -negative specimens from 92 symptomatic individuals earlier during the COVID-19 pandemic (March–June 2021) were distributed to 3 of the 10 sites and worked into the daily workflow of sites for testing.

Clinical performance evaluation using nasopharyngeal swab specimens

The clinical performance of the **cobas**® SARS-CoV-2 test for the detection of SARS-CoV-2 from healthcare-provider collected NPS specimens collected in UTM/UVT was evaluated based on test results from a total of 1876 individual fresh and frozen (23 prospective frozen SARS-CoV-2-positive NPS specimens were tested at sites; one frozen negative specimen was included for each frozen positive specimen) NPS specimens. Of these, 2 NPS specimens were non-evaluable due to invalid/failed tests. The remaining 1874 NPS specimens were evaluable and included in the clinical performance evaluation of **cobas**® SARS-CoV-2.

As shown in Table 16 for symptomatic individuals, 125 NPS specimens tested positive for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 test on **cobas**® Liat® System and the composite comparator; six SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**® SARS-CoV-2 test. A total of 539 NPS specimens tested negative for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 test and the composite comparator; three SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**® SARS-CoV-2 test.

For NPS specimens prospectively collected from symptomatic individuals, **cobas**® SARS-CoV-2 demonstrated 95.4% PPA (125/131; 95% score CI: 90.4%-97.9%) and 99.5% NPA (539/542; 95% score CI: 98.4%-99.8%).

Table 16 Clinical performance comparison with the composite comparator method – NPS specimens from symptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas® SARS-CoV-2 on **cobas**® Liat® System **Nasopharyngeal Swab**	Positive	125	3
	Negative	6	539

PPA	95.4% (95% CI: 90.4% - 97.9%)
NPA	99.5% (95% CI: 98.4% - 99.8%)

As shown in Table 17 for asymptomatic individuals, 52 NPS specimens tested positive for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 test on **cobas**® Liat® System and the composite comparator; two SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**® SARS-CoV-2 test. A total of 1142 NPS specimens tested negative for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 test and the composite comparator; five SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**® SARS-CoV-2 test. For NPS specimens prospectively collected from asymptomatic individuals, **cobas**® SARS-CoV-2 demonstrated 96.3% PPA (52/54; 95% score CI: 87.5%-99.0%) and 99.6% NPA (1142/1147; 95% score CI: 99.0%-99.8%).

Table 17 Clinical performance comparison with the composite comparator method – NPS specimens from asymptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas® SARS-CoV-2 on **cobas**® Liat® System **Nasopharyngeal Swab**	Positive	52	5
	Negative	2	1142

PPA	96.3% (95% CI: 87.5% - 99.0%)
NPA	99.6% (95% CI: 99.0% - 99.8%)

Clinical performance evaluation using nasal swab specimens

The clinical performance of the **cobas**® SARS-CoV-2 test for the detection of SARS-CoV-2 from nasal (NS) specimens collected in UTM/UVT was evaluated from a total of 1950 individual fresh and frozen (twenty-three prospective frozen SARS-CoV-2-positive NS specimens were tested at sites; one frozen negative specimen was included for each frozen positive specimen) NS specimens; NS specimens were comprised of either healthcare provider-collected (49.6%) or self-collected swabs (50.4%). Overall, 77 NS specimens were non-evaluable due to not being tested, protocol deviation, or invalid/failed tests. The remaining 1873 NS specimens (including 1 indeterminate result) were evaluable and included in the clinical performance evaluation of **cobas**® SARS-CoV-2.

As shown in Table 18 for symptomatic individuals, 129 NS specimens tested positive for SARS-CoV-2 with both the

cobas® SARS-CoV-2 test on **cobas**® Liat® System and the composite comparator; five SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**® SARS-CoV-2 test. A total of 539 NS specimens tested negative for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 test and the composite comparator; one SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**® SARS-CoV-2 test.

Overall, for NS specimens prospectively collected from symptomatic individuals, **cobas**® SARS-CoV-2 demonstrated 96.3% PPA (129/134; 95% score CI: 91.6%-98.4%) and 99.8% NPA (539/540; 95% score CI: 99.0%-100.0%).

Table 18 Clinical performance comparison with the composite comparator method – NS specimens from symptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas® SARS-CoV-2 on **cobas**® Liat® System **Nasal Swab**	Positive	129	1
	Negative	5	539

PPA	96.3% (95% CI: 91.6% - 98.4%)
NPA	99.8% (95% CI: 99.0% - 100.0%)

Note: The nasal swabs were comprised of healthcare provider-collected nasal swab specimens and nasal swab specimens self-collected on-site with healthcare provider instructions.

As shown in Table 19 for asymptomatic individuals, 45 NS specimens tested positive for SARS-CoV-2 with both the cobas® SARS-CoV-2 test on cobas® Liat® System and the composite comparator; five SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the cobas® SARS-CoV-2 test. A total of 1147 NS specimens tested negative for SARS-CoV-2 with both the cobas® SARS-CoV-2 test and the composite comparator; one SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the cobas® SARS-CoV-2 test.

Overall, for NS specimens prospectively collected from asymptomatic individuals, **cobas**® SARS-CoV-2 demonstrated 90.0% PPA (45/50; 95% score CI: 78.6%-95.7%) and 99.9% NPA (1147/1148; 95% score CI: 99.5%-100.0%).

Table 19 Clinical performance comparison with the composite comparator method – NS specimens from asymptomatic individuals

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas® SARS-CoV-2 on **cobas**® Liat® System **Nasal Swab**	Positive	45	1
	Negative	5	1147

PPA	90.0% (95% CI: 78.6% - 95.7%)
NPA	99.9% (95% CI: 99.5% - 100.0%)

Note: The nasal swabs were comprised of healthcare provider-collected nasal swab specimens and nasal swab specimens self-collected on-site with healthcare provider instructions.

Failure codes

The result report may contain failure codes as described in Table 20, depending on potential run failures. For any questions, please contact your Roche Service representative.

Table 20 Failure codes and definitions

Failure Code Summary Failure Codes	Failure Code Summary Sample	Failure Code Summary Negative Control	Failure Code Summary Positive Control
g0*	IPC out of range. Repeat run.	IPC out of range. Repeat run.	IPC out of range. Repeat run.
g1	IPC out of range. Repeat run.	IPC out of range. Repeat run.	IPC out of range. Repeat run.
g2	IPC out of range. Repeat run.	IPC out of range. Repeat run.	IPC out of range. Repeat run.
g3	IPC out of range. Repeat run.	IPC out of range. Repeat run.	IPC out of range. Repeat run.
g4	IPC out of range. Repeat run.	IPC out of range. Repeat run.	IPC out of range. Repeat run.
x4	SARS-CoV-2 target out of range. Repeat run.	N/A	N/A
FP	N/A	SARS-CoV-2 target out of range. Repeat run.	N/A
r1	N/A	N/A	SARS-CoV-2 target out of range. Repeat run.
r2	N/A	N/A	SARS-CoV-2 target out of range. Repeat run.
r3	N/A	N/A	SARS-CoV-2 target out of range. Repeat run.
r4	N/A	N/A	SARS-CoV-2 target out of range. Repeat run.

Note: * Failure code g0 does not appear for Positive Control.

CLIA Waiver study

Clinical performance characteristics of the **cobas**® SARS-CoV-2 test were evaluated in a multi-site prospective study during Feb to June 2022 respiratory season in the U.S. Ten (10) sites throughout the U.S. participated in the clinical study. The sites consisted of emergency rooms, urgent care clinics, outpatient clinics, physicians' offices and drive through COVID-19 testing sites. All the sites qualified as representative of CLIA waived intended use sites for this device.

There were a total of 30 operators representative of intended CLIA waived users across the ten clinical testing sites, with between 2 to 5 operators per site. The participants consisted of medical staff personnel providing patient care and included medical assistants, nurses, office managers, study coordinators, phlebotomists, and others. The test operators who participated in the study were untrained in the use of the **cobas**® SARS-CoV-2 test and had no hands-on experience with conducting diagnostic testing in a clinical laboratory.

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, weak positive samples and obtain accurate results. This was evaluated as a part of the reproducibility study.

A total of 268 negative samples and 266 weak positive samples were tested by two untrained operators at each of the three sites. The expected result for the true negative panel member is "Not Detected," while the expected result for the low positive panel member is "Detected." Percent agreement with expected result, mean Ct, Ct SD, and Ct %CV are shown in table below.

Table 21 Results for near cutoff study

Sample	Total number of valid test runs	Site 1 Agreement with Expected Results	Site 2 Agreement with Expected Results	Site 3 Agreement with Expected Results	All sites Avg. Ct ± SD (%CV)	All sites Agreement(n/N) and (95% CI)
Negative	268	100.0% (90/90)	100.0% (88/88)	98.9% (89/90)	-	99.6% (267/268) (97.9%-99.9%)
SARS-CoV-2 Low Positive	266	100.0% (89/89)	100.0% (90/90)	97.7% (85/87)	33.4±0.96 (2.9%)	99.2% (264/266) (97.3%-99.8%)

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

Key test features

Sample type	Nasopharyngeal and Nasal swab samples collected in the Copan UTM-RT System or the BD™ UVT System or Thermo Fischer™ Remel (M4®, M4RT®, M5®, M6®), and premeasured 3 mL 0.9% or 0.85% physiological saline.
Minimum amount of sample required	Approximately 0.2 mL
Test duration	Results are available within approximately 20 minutes after loading the sample on the instrument.

Symbols

The following symbols are used in labeling for Roche PCR diagnostic products.

Table 22 Symbols used in labeling for Roche PCR diagnostics products

Age/DOB Age or Date of Birth	Device not for near-patient testing	QS IU/PCR QS IU per PCR reaction, use the QS International Units (IU) per PCR reaction in calculation of the results.
SW Ancillary Software	Device not for self-testing	
Assigned Range [copies/mL] Assigned Range (copies/mL)	Distributor *(Note: The applicable country/region may be designated beneath the symbol)*	SN Serial number
Assigned Range [IU/mL] Assigned Range (IU/mL)	Do not re-use	Site Site
EC REP Authorized representative in the European Community	Female	Procedure Standard Standard Procedure
BARCODE Barcode Data Sheet	For IVD performance evaluation only	STERILE EO Sterilized using ethylene oxide
LOT Batch code	GTIN Global Trade Item Number	Store in dark
Biological risks	Importer	Temperature limit
REF Catalogue number	IVD In vitro diagnostic medical device	TDF Test Definition File
CE CE marking of conformity; this device is in conformity with the applicable requirements for CE marking of an in vitro diagnostic medical device	LLR Lower Limit of Assigned Range	This way up
	Male	Procedure UltraSensitive Ultrasensitive Procedure
Collect Date Collect date	Manufacturer	UDI Unique Device Identifier
Consult instructions for use	CONTROL − Negative control	ULR Upper Limit of Assigned Range
Σ Contains sufficient for <n> tests	NON STERILE Non-sterile	Urine Fill Line Urine Fill Line
CONTENT Content of kit	Patient Name	Rx Only US Only: Federal law restricts this device to sale by or on the order of a physician.
CONTROL Control	Patient number	Use-by date
Date of manufacture	Peel here	
Device for near-patient testing	CONTROL + Positive control	
Device for self-testing	QS copies / PCR QS copies per PCR reaction, use the QS copies per PCR reaction in calculation of the results.	

Technical support

For technical support (assistance) please reach out to your local affiliate:
https://www.roche.com/about/business/roche_worldwide.htm

Manufacturer and distributor

Table 23 Manufacturer and distributor

	Roche Molecular Systems, Inc. 1080 US Highway 202 South Branchburg, NJ 08876 USA www.roche.com Made in USA
Distributed by	Roche Diagnostics 9115 Hague Road Indianapolis, IN 46250-0457 USA (For Technical Assistance call the Roche Response Center toll-free: 1-800-526-1247)

Trademarks and patents

See https://diagnostics.roche.com/us/en/about-us/patents

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Document revision

Document Revision Information	
Doc Rev. 4.0 02/2024	Added Non-clinical and Clinical Performance study data for regulatory submission. Intended use revised for 510(k) clearance. Removed references to emergency use authorization and indicated the 'CLIA-waived' status. Updated **Transport and storage** section to add a specimen media statement. Please contact your local Roche Representative if you have any questions.