cobas® SARS-CoV-2

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

For in vitro diagnostic use

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 RT-PCR assay intended for the rapid in vitro qualitative detection of SARS-CoV-2 in self-collected nasal swabs (collected in a healthcare setting with instruction by a healthcare provider) and healthcare provider-collected nasopharyngeal and nasal swabs from either individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider or from individuals without symptoms or other reasons to suspect COVID-19.

cobas® SARS-CoV-2 is intended for use in the detection of SARS-CoV-2 in clinical specimens. SARS-CoV-2 viral RNA is generally detectable in upper respiratory specimens during the acute phase of infection. Positive results are indicative of active infection but do not rule out co-infection with other pathogens not detected by the test. Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The agent detected may not be the definite cause of disease.

Negative results do not preclude infection from SARS-CoV-2 and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and/or epidemiological information.

cobas® SARS-CoV-2 is intended for use by health professionals or trained operators who are proficient in using the **cobas**® Liat® System in Near Patient Testing, Point of Care (POC) or in a clinical laboratory setting.

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. 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 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 **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.	N/A
Proteinase K	100% Proteinase K	N/A
cobas® Liat® Magnetic Glass Particles	Magnetic Glass Particles	N/A

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® Lysis Buffer	Citric acid, sodium phosphate, 42.6% guanidinium isothiocyanate[b], 5% decaethylene glycol monododecyl ether[b], dithiothreitol	 **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 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.	N/A

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® 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.	N/A
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.	N/A

[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) 1 **cobas**® transfer pipette pack (12 pipettes/pack - P/N 09329676001) 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
cobas® SARS-CoV-2 Quality Control Kit	2-8°C	Stable until the expiration date indicated

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 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 220528 3C047N
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-aliquotted 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

Note: If the viral transport media and saline listed in Table 4 are not available, CLIA certified moderate and high complexity laboratories only may prepare and package equivalent 3 mL of physiological saline (0.9% or 0.85%) for use with **cobas**® SARS-CoV-2 assay.

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 v1.0 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.
- Before using **cobas**® SARS-CoV-2, operator should carefully read Instructions For Use (IFU) and the **cobas**® Liat® System User Guide.
- Treat all biological specimens, including used **cobas**® SARS-CoV-2 assay tubes and transfer pipettes, as if capable of transmitting infectious agents. It is often impossible to know which specimens might be infectious; all biological specimens should be treated with universal precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention, Clinical and Laboratory Standards Institute and World Health Organization.[12-16]
- 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-aliquotted 3 mL 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 pipettes 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.
- In EU: Inform your local competent authority about any serious incidents which may occur when using this assay.

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 specimen using a sterile flocked swab with a synthetic tip (e.g., Dacron, nylon, or rayon) according to applicable manufacturer instructions and/or standard collection technique using 3 mL of viral transport media. If the viral transport media listed in Table 4 are not available an alternative 0.9% or 0.85% physiological saline solution can be used.

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 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.
- Specimen 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-RT® or UVT, M4, M4RT, M5, M6, or 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. 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.

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. **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 or QC 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 barcode on the Package Insert ID 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 **cobas**® SARS-CoV-2 assay tube barcode
5	Scan or enter sample ID
6	Add specimen to **cobas**® SARS-CoV-2 assay tube using transfer pipette and re-cap the tube
7	Re-scan **cobas**® SARS-CoV-2 assay tube barcode
8	Start run
9	Review results*
10	Unload and dispose used **cobas**® SARS-CoV-2 assay tube

*Refer to **cobas**® Liat® System User Guide for details of result uploading to LIS/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 Positive Control tube[2]
□ 1 **cobas**® SARS-CoV-2 assay tube from this lot[1]	□ 1 **cobas**® SARS-CoV-2 assay tube from this lot[1]
□ 1 transfer pipette[1 or 2]	□ 1 transfer pipette[1 or 2]
□ Package Insert Barcode card[1]	□ Positive Control Barcode on the Control Kit Barcode Card[2]
□ Negative Control Barcode on the Control Kit Barcode Card[2]	

[1]Contained in **cobas**® Liat® Assay Kit

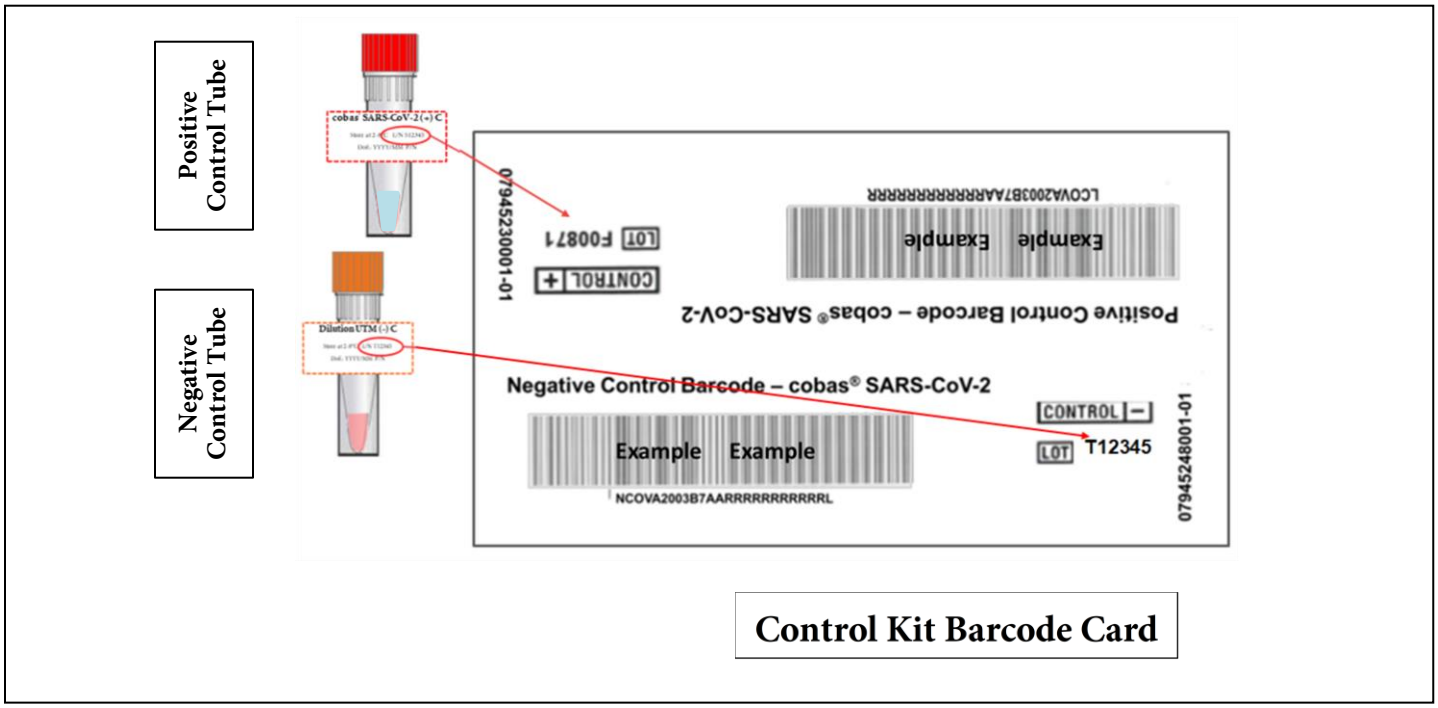
- Package Insert ID Barcode Card: This barcode is lot-specific; match the lot number next to the barcode with the lot number on the **cobas**® SARS-CoV-2 assay tubes.

[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 Label 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 negative control run.
- Match the lot numbers (L/N) of the Positive Control tube label for **cobas**® SARS-CoV-2 to the lot number(LOT) of the Positive Control Barcode Label on the Control Kit Barcode Card. Use the Positive Control Barcode (on the Control Kit Barcode Card) as the sample ID when performing positive control run.

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



Assay tube Lot Validation workflow

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

   Note: You may be prompted to confirm you have read the User Manual (i.e., cobas® Liat® System User Guide).
5. Select "**Assay Menu**" on the main menu of a **cobas**® Liat® Analyzer.
6. Select "**New Lot**" at the bottom of the list.
7. When prompted to **Scan the Insert ID**, select "**Scan**" and scan the **cobas**® SARS-CoV-2 Package Insert ID 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 the Negative Control ID**, select "**Scan**" and scan the Negative Control 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. Select "**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 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, select **"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. Select "**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, select "**OK**" and then select "**Back**" to return to Main menu. If the result is rejected, repeat the **cobas**® SARS-CoV-2 Positive Control test. If repeated control runs do not produce the expected results, contact your local Roche representative.

23. Select "**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. Select **"Login"** on the screen of the **cobas**® Liat® Analyzer.
3. Enter user name when prompted, select **"OK"**.
4. Enter user password when prompted, select **"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, select "**Run Assay**".
6. Open up a **cobas**® SARS-CoV-2 assay tube pouch and take out the assay tube. When prompted to **Scan Liat Tube ID,** select **"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 the sample ID**, select "**Scan**" to scan the sample barcode. In the case that the sample cannot be scanned, select "**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 to transfer specimen.
10. 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.
11. 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.

12. 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.

13. 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.

14. Select **"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.

15. 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.

16. 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.

17. 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 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.

18. Select **"Report"** to see the Result Report. If applicable, select **"Print"** to print the report.

19. Select **"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 barcode. 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 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.
Assay Aborted by system		Run failed or aborted by system. Repeat assay with same sample.
Assay Aborted by Running Script		Run failed or aborted by script. Repeat assay with same sample.
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

- **cobas**® SARS-CoV-2 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 nasal and nasopharyngeal 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® 3 mL Sterile Normal Saline (0.85%). Testing of other sample or media types may lead to inaccurate results.
- 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.
- 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.
- 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.

Non-clinical performance evaluation

Key performance characteristics

Analytical sensitivity

The analytical sensitivity (Limit of detection or 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.

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 an approximately equal numbers of replicates per dilution series. The LoD was determined by probit analysis of the hit rates at each concentration level.

The results of the hit rate and LoD are shown in Table 9 and Table 10 below.

Table 9 Hit rate and mean Ct results of SARS-CoV-2 LoD determination

Strain	Concentration [IU/mL]	Valid Positive Results	Total Valid Results	Hit Rate [%]	Mean Ct*
WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146)	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

Table 10 LoD of SARS-CoV-2 as determined by Probit Analysis

WHO International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146)	Probit Predicted LoD (IU/mL)
	24 (95% CI: 19 – 38)

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.

The lowest concentration level with observed hit rates greater than or equal to 95% was 0.012 $TCID_{50}$/mL (12 copies/mL) as shown in Table 11. The probit predicted 95% hit rate was 0.010 TCID50/mL (10 copies/mL) for SARS-CoV-2 as shown in Table 12.

Table 11 LoD determination using USA-WA1/2020 Strain

Strain	Concentration [$TCID_{50}$/mL]	Concentration [copies/mL]*	Total valid results	Hit rate [%]	Mean Ct**
USA-WA1/2020 (stock concentration 3.16E+06 $TCID_{50}$/mL)	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 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.

Table 12 Probit predicted 95% Hit Rates using USA-WA1/2020 strain

Strain	Probit Predicted 95% Hit Rate [$TCID_{50}$/mL]
USA-WA1/2020 (stock concentration 3.16E+06 $TCID_{50}$/mL)	0.010 $TCID_{50}$/mL, 10 copies/mL (95% CI: 0.007 - 0.029 $TCID_{50}$/mL) (95%CI: 7 – 29 copies/mL)

Reactivity/inclusivity

The inclusivity study evaluates the assay ability to detect SARS-CoV-2 isolates/variants. In this study, twelve (12) SARS-CoV-2 isolates/variants were tested. The isolates/variants were either inactivated viruses or extracted viral RNA diluted into pooled clinical negative nasopharyngeal swab matrix. The isolates/variants tested in the study and the concentrations that they can be detected are listed in Table 13.

Table 13 Summary of SARS-CoV-2 Inclusivity Testing

Isolate/Variant	Pango Lineage	WHO Label	Test Concentration (cp/mL)
Germany/BavPat1/2020	B	N/A	4.00E+01
Italy-INMI1	not listed	N/A	5.00E+00
Hong Kong/VM20001061/2020	A	N/A	2.00E+01
California Variant	B.1.427	Epsilon	4.00E+01
California Variant	B.1.429	Epsilon	4.00E+01
UK variant	B.1.1.7	Alpha	5.00E+00
South Africa Variant	B.1.351	Beta	2.00E+01
Brazilian Variant	P.1	Gamma	4.00E+01
India Variant	B.1.617.2	Delta	1.20E+02
New York Variant	B.1.526	Iota	1.20E+02
India Variant	B.1.617.1	Kappa	4.00E+01
USA/MD-HP20874/2021	B.1.1.529	Omicron	4.00E+01

Cross reactivity and Microbial Interference

Cross-reactivity and microbial interference of **cobas**® SARS-CoV-2 were evaluatesd 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 with spiked 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 14).

None of the organisms tested interfered with **cobas**® SARS-CoV-2 performance by generating false positive results.

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. Please note that in presence of SARS-coronavirus (SARS-CoV-1) at 1e5 pfu/mL, 3x LoD concentrations of SARS-CoV-2 was not detected at 3x LoD, 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 14 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
	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
		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 Coronavirus did not cause false positive results at 1e5 pfu/mL and 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 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 15 substances at the concentrations tested did not interfere in the detection of SARS-CoV-2.

Table 15 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

Clinical performance evaluation

The clinical performance of the **cobas**® SARS-CoV-2 assay was separately evaluated using unpaired retrospective and paired prospective clinical nasopharyngeal swab (NPS) and nasal swab (NS) specimens collected from both individuals suspected of respiratory viral infection consistent with COVID-19 as well as screened individuals without symptoms or other reason to suspect COVID-19. Testing of clinical samples was performed with the **cobas**® SARS-CoV-2 assay 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-authorized laboratory-based RT-PCR EUA assays (composite comparator method).

Prospective clinical specimens were collected and tested February–June 2022. In total, prospectively collected specimens from 1862 evaluable individuals were included in the analysis population for the evaluation of **cobas**® SARS-CoV-2. Of this population, 640 individuals had signs and symptoms of respiratory infection consistent with COVID-19 (34.4%), 419 individuals were suspected of SARS-CoV-2 infection due to recent exposure or other reason (22.5%), and 803 individuals were without symptoms or other reasons to suspect COVID-19 and tested for screening purposes (43.1%). Additionally for each specimen type, 23 each retrospective known SARS-CoV-2-positive and -negative specimens obtained 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 assay for the detection of SARS-CoV-2 from healthcare-provider collected prospective and retrospective nasopharyngeal (NPS) specimens collected in UTM/UVT was evaluated from a total of 1876 individual NPS specimen test results. Twenty-three retrospective known SARS-CoV-2-positive NPS specimens were tested at sites; one retrospective negative specimen was included for each retrospective positive specimen. 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, 177 NPS specimens tested positive for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 assay on **cobas**® Liat System and the composite comparator; eight SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**® SARS-CoV-2 assay. A total of 1681 NPS specimens tested negative for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 test and the composite comparator; eight SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**® SARS-CoV-2 assay. All discordant SARS-CoV-2 results showed late Ct values, which are indicative of NPS specimens from individuals with viral loads near or below the limit of detection of both **cobas**® SARS-CoV-2 and the composite comparator methods.

Overall for SARS-CoV-2, the results of the clinical performance evaluation using NPS specimens demonstrated 95.7% positive percent agreement and 99.5% negative percent agreement as compared to the composite comparator method.

For NPS specimens prospectively collected from symptomatic subjects, **cobas**® SARS-CoV-2 demonstrated 94.4% PPA (102/108; 95% score CI: 88.4%-97.4%) and 99.4% NPA (516/519; 95% score CI: 98.3%-99.8%). For NPS specimens prospectively collected from asymptomatic subjects, **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 16 Clinical performance comparison with the composite comparator method – NPS specimens

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas® SARS-CoV-2 on **cobas**® Liat® System **Nasopharyngeal Swab (NPS)**	Positive	177	8
	Negative	8[a]	1681

PPA	95.7% (95% CI: 91.7% - 97.8%)
NPA	99.5% (95% CI: 99.1% - 99.8%)

[a]Of these, three specimens yielded a positive result upon retesting with **cobas**® SARS-CoV-2 on the **cobas**® Liat System.

Clinical performance evaluation using nasal swab specimens

The clinical performance of the **cobas**® SARS-CoV-2 assay for the detection of SARS-CoV-2 from prospective and retrospective nasal (NS) specimens collected in UTM/UVT was evaluated from a total of 1950 individual NS specimen test results; NS specimens were comprised of either healthcare provider-collected or self-collected swabs. Twenty-three retrospective known SARS-CoV-2-positive NS specimens were tested at sites; one retrospective negative specimen was included for each retrospective positive specimen. Of these, 77 NS specimens were non-evaluable due to not being tested, protocol deviation, or invalid/failed tests. The remaining 1873 NS specimens were evaluable and included in the clinical performance evaluation of **cobas**® SARS-CoV-2.

As shown in Table 17, 174 NS specimens tested positive for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 assay on **cobas**® Liat System and the composite comparator; ten SARS-CoV-2-positive specimens tested negative for SARS-CoV-2 with the **cobas**® SARS-CoV-2 assay. A total of 1686 NS specimens tested negative for SARS-CoV-2 with both the **cobas**® SARS-CoV-2 assay and the composite comparator; two SARS-CoV-2-negative specimens tested positive for SARS-CoV-2 with the **cobas**® SARS-CoV-2 assay. Eleven of the 12 discordant SARS-CoV-2 results showed late Ct values, which are indicative of NS specimens from individuals with viral loads near or below the limit of detection of both **cobas**® SARS-CoV-2 and the composite comparator methods.

Overall for SARS-CoV-2, the results of the clinical performance evaluation using NS specimens demonstrated 94.6% positive percent agreement (PPA) and 99.9% negative percent agreement (NPA) as compared to the composite comparator method.

For healthcare-provider collected NS specimens, **cobas**® SARS-CoV-2 demonstrated 92.2% PPA (83/90; 95% score CI: 84.8%-96.2%) and 99.9% NPA (835/836; 95% score CI: 99.3%-100.0%) as compared to the composite comparator method for SARS-CoV-2 detection. For self-collected NS specimens, **cobas**® SARS-CoV-2 demonstrated 96.8% PPA (91/94; 95% score CI: 91.0%-98.9%) and 99.9% NPA (851/852; 95% score CI: 99.3%-100.0%) as compared to the composite comparator method for SARS-CoV-2 detection.

For NS specimens prospectively collected from symptomatic subjects, **cobas**® SARS-CoV-2 demonstrated 95.5% PPA (106/111; 95% score CI: 89.9%-98.1%) and 99.8% NPA (516/517; 95% score CI: 98.9%-100.0%). For NS specimens prospectively collected from asymptomatic subjects, **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 17 Clinical performance comparison with the composite comparator method – NS specimens

		Composite Comparator Method SARS-CoV-2 Result	
		Positive	Negative
cobas® SARS-CoV-2 on **cobas**® Liat® System **Nasal Swab (NS)**	Positive	174	2
	Negative	10[a]	1686

PPA	94.6% (95% CI: 90.3% - 97.0%)
NPA	99.9% (95% CI: 99.6% - 100.0%)

[a]Of these, six specimens yielded a positive result upon retesting with **cobas**® SARS-CoV-2 on the **cobas**® Liat System.

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. 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 18.

Table 18 SARS-CoV-2 reproducibility

Number of Valid Test Runs		Negative	SARS-CoV-2 Low Positive	SARS-CoV-2 Moderate Positive
		268	266	268
Ct	Mean	-	33.4	32.5
	SD	-	0.96	0.54
	CV (%)	-	2.9	1.7
Site	1	100.0% (90/90)	100.0% (89/89)	100.0% (88/88)
	2	100.0% (88/88)	100.0% (90/90)	100.0% (90/90)
	3	98.9% (89/90)*	97.7% (85/87)	100.0% (90/90)
Overall Hit Rate	Agreement (n/N)	99.6% (267/268)	99.2% (264/266)	100.0% (268/268)
	95% CI	97.9% - 99.9%	97.3% - 99.8%	98.6% - 100.0%

*One negative sample yielded a "Detected" result; remnant volume from this negative sample was retested twice using the same assay tube lot and yielded.

a "Not Detected" result as expected

Failure codes

The result report may contain failure codes as described in Table 19, depending on potential run failures. For any questions, please contact your Roche Service representative.

Table 19 Failure codes and definitions

Failure Code Summary			
Failure Codes	**Sample**	**Negative Control**	**Positive Control**
g0*	IPC out of range. Repeat run.	IPC out of range. Repeat run.	IPC out of range. Repeat run.
g1			
g2			
g3			
g4			
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			
r3			
r4			

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

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 Fisher™ Remel (M4®, M4RT®, M5®, M6®), and 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 20 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 For USA: Caution: 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 importer

Table 21 Manufacturer and importer

Roche Molecular Systems, Inc.
1080 US Highway 202 South
Branchburg, NJ 08876, USA
www.roche.com

Made in USA

Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany

Trademarks and patents

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

Copyright

IVD

EC REP Roche Diagnostics GmbH
Sandhofer Str. 116
68305 Mannheim
Germany

CE
2797

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Document revision

Document Revision Information	
Doc Rev. 3.0 02/2024	Updated to include IVDR requirements. Please contact your local Roche Representative if you have any questions.
Doc Rev. 4.0 06/2024	Updated **cobas**® SARS-CoV-2 hazard information. Updated transfer pipettes included in the **cobas**® SARS-CoV-2 Quality Control Kit to cobas® transfer pipette pack (P/N 9329676001). Removed Rx Only from front page. Updated the harmonized symbol page. Please contact your local Roche Representative if you have any questions.

The summary of safety and performance report can be found using the following link:
https://ec.europa.eu/tools/eudamed