cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test

For in vitro diagnostic use

For Rx Use Only

CLIA Complexity: WAIVED

cobas® liat SARS-CoV-2, Influenza A/B & RSV	P/N: 09731261190
cobas® liat SARS-CoV-2, Influenza A/B & RSV control kit	P/N: 09731270190

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

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

Intended use

The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test is an automated rapid multiplex real-time reverse transcription polymerase chain reaction (RT-PCR) test intended for the simultaneous qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus, influenza B virus and respiratory syncytial virus (RSV) nucleic acids in anterior nasal (nasal) and nasopharyngeal swab specimens from individuals exhibiting signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2, influenza and RSV can be similar. This test is intended to aid in the differential diagnosis of SARS-CoV-2, influenza A, influenza B, and RSV infections in humans and is not intended to detect influenza C virus infections.

Nucleic acids from the viral organisms identified by this test are generally detectable in nasopharyngeal and nasal swab specimens during the acute phase of infection. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory tract infection are indicative of the presence of the identified virus, and aid in diagnosis if used in conjunction with other clinical and epidemiological information, and laboratory findings.

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

Positive results do not rule out coinfection with other organisms. The organism(s) detected by the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus, or RSV infections.

Summary

Effective diagnosis and differentiation of SARS-CoV-2, influenza A, influenza B, and RSV infections from one another and from other respiratory pathogens is needed to address a substantial burden of illness. [1,2] The global seasonality of influenza and RSV epidemics overlap, with peaks of infectious activity occurring in the respective winter months for temperate climates in the Northern and Southern hemispheres.[3] The seasonality and symptoms of COVID-19 also overlap with other respiratory diseases, with the clinical manifestation ranging from asymptomatic or mild "influenza-like" illness to more severe and life-threatening disease.[4,5]

To allow for rapid medical management and effective infection control, a fast, accurate, user-friendly and near-patient diagnostic solution is needed to detect and differentiate SARS-CoV-2, influenza A, influenza B, and RSV in patients of all ages with acute respiratory symptoms.[6,7] Prompt and accurate detection of the causative pathogen can help to target the use of antivirals and implementation of infection control measures, avoid inappropriate antibiotic use, reduce ancillary testing and hospitalizations, and identify local outbreaks of disease sooner.[8] **cobas® liat** SARS-CoV-2, Influenza A/B & RSV uses real-time PCR to rapidly detect viral RNA from both nasopharyngeal swab (NPS) and anterior nasal swab (ANS) specimens.

Test principle

The test is performed on the **cobas® liat** analyzer which automates and integrates sample purification, nucleic acid amplification, and detection of the target sequence in biological samples using real-time RT-PCR assays. The assay targets

both the ORF1 a/b non-structural region and membrane protein gene that are unique to SARS-CoV-2, a well-conserved region of the matrix gene of influenza A (Flu A target), the nonstructural protein 1 (NS1) gene of influenza B (Flu B target), and the matrix gene of RSV (RSV target). An Internal Control (IC) is included to control for adequate processing of the target virus through all steps of the assay process and to monitor the presence of inhibitors in the RT-PCR processes.

The sample to result time is approximately 20 minutes.

Precautions and warnings

- For in vitro diagnostic use.
- For prescription use only.
- 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® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test, operator should carefully read all testing instructions, warnings, and precautions in the Instructions for Use and the **cobas® liat** system User Guide.
- Treat all biological samples, including used **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tubes and transfer pipettes, as if capable of transmitting infectious agents. All biological samples should be treated with universal precautions. Guidelines for sample handling are available from the U.S. Centers for Disease Control and Prevention, Clinical and Laboratory Standards Institute, and the World Health Organization.[9,10]
- If infection with a novel SARS-CoV-2 or influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, positive results should be reported to state, local, or federal health departments according to local reporting requirements. Specimens should be collected using appropriate infection control precautions for novel virulent viruses sent to local health departments for testing. Virus culture should not be attempted in these cases unless a BSL-3 and BSL-3+ facility is available to receive and culture specimens.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- On request, Safety Data Sheets (SDS) are available from your local Roche representative.
- Use only the transfer pipettes contained in the **cobas® liat** transfer pipette pack. Use of alternative transfer pipettes may lead to invalid results.
- Carefully adhere to the procedures specified in this Instructions for Use document. Wear laboratory gloves, laboratory coat, and eye protection when handling samples and reagents. Change gloves before removing transfer pipette from the **cobas® liat** transfer pipette pack and after handling each sample or control. After handling samples and kit reagents, remove gloves and wash hands thoroughly.
- Due to the high sensitivity of the assays run on the **cobas® liat** analyzer, contamination of the work area with previous positive samples or the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV positive control may cause false positive results. Handle samples with caution. If spills occur on the **cobas® liat** analyzer, follow the appropriate instructions in the **cobas® liat** system User Guide to clean.

- 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% 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.

Sample collection, transport, and storage

See Table 4 for a list of collection kits for use with **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test. Follow the instructions for collecting all swab samples in their respective collection kit instructions for use (IFU).

Sample collection

- Collect specimen 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 (VTM) or 0.9% saline.

Transport and storage

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

- Swab samples should be tested as soon as possible. If needed, specimens may be stored at 15-30 °C for up to 4 hours after collection, or at 2-8 °C for up to 72 hours. If needed, specimens collected in VTM may be stored frozen (-70 °C or colder) if testing within 72 hours is not possible.
  Note: Specimens collected in saline should not be frozen.
- Once sample has been transferred into a **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube, start the run on the **cobas® liat** analyzer as soon as possible but no later than 4 hours at room temperature (15-30 °C).

Materials required, storage and handling

The materials provided for **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test can be found in Table 1 and Table 2. Reagent handling and storage can be found in Table 3. Materials required, but not provided can be found in Table 4 and Instrumentation and software required Table 5.

cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test reagents and controls

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

Table 1: cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test
Store at 2-8 °C
20 tests (P/N 09731261190)
2 **cobas® liat** transfer pipette packs (12 pipettes/pack - P/N 09329676001)
1 package insert barcode card

Reagents in cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic test assay tube	Reagent ingredients	Safety symbol and warning[a]
cobas® liat Internal Control	Tris buffer, EDTA, <0.02% non-target related armored RNA construct containing primer and probe specific sequence regions, <0.1% Sodium azide	N/A
cobas® liat Magnetic Glass Particles	Magnetic Glass Particles	N/A
cobas® liat Lysis Buffer	Citric acid, Sodium phosphate, <40% guanidinium thiocyanate[b], Dibasic sodium phosphate, Dithiothreitol Brij® 35	 **DANGER** H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H412: Harmful to aquatic life with long lasting effects. EUH032: Contact with acids liberates very toxic gas. EUH071: Corrosive to the respiratory tract. P273: Avoid release to the environment. P280: Wear protective gloves/protective clothing/ eye protection/face protection/hearing protection. P301 + P330 + P331: IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor. P305 + P351 + P338 + P310: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. 593-84-0 Guanidinium thiocyanate

Reagents in cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic test assay tube	Reagent ingredients	Safety symbol and warning[a]
cobas® liat Wash Buffer	Sodium Citrate Dihydrate, 0.1% Methyl P-Hydroxybenzoate	N/A
cobas® liat Elution Buffer	Trehalose, Tris buffer, BSA, Magnesium sulfate, 0.01% ProClin® 300 preservative[b]	N/A
cobas® liat Master Mix-1	Tricine buffer, Potassium acetate, Potassium hydroxide, EDTA, DMSO, 0.09% Sodium azide, Tween 20, Glycerol, Recombinant human serum albumin, dATP, dCTP, dGTP, dUTP, Target and Internal Control primers, UNG	N/A
cobas® liat Master Mix-2	Trizma-base, DTT, EDTA, 0.01% Tween-80, < 0.03% Tween-20, Glycerol, Potassium chloride, <0.01% MMLV Reverse Transcriptase	N/A
cobas® liat Master Mix-3	Tricine, Potassium acetate, Potassium hydroxide, EDTA, 0.09% Sodium azide, 0.06 % Tween-20, recombinant human serum albumin, < 0.008% Target and Internal Control primers, < 0.01% fluorescent target and Internal Control probes, Aptamer, < 0.03% Z05 DNA polymerase	N/A

[a]Product safety labeling follows EU GHS guidance and US FDA regulations.
[b]Hazardous substance or mixture

Table 2: cobas® liat SARS-CoV-2, Influenza A/B & RSV control kit
Store at 2-8°C
(P/N 09731270190)
1 Control Kit Barcode Card

Kit components	Reagent ingredients	Quantity per kit	Safety symbol and warning[a]
cobas® liat SARS-CoV-2, Influenza A/B & RSV positive control (SARS2 Flu A/B & RSV (+) C) (P/N 09747974001)	Tris buffer, EDTA < 0.003% Poly rA (synthetic), < 0.001% non-infectious armored RNAs containing SARS-CoV-2, influenza A influenza B, & RSV sequences, < 0.1% Sodium azide	3 X 0.3 mL	N/A
cobas® liat Neg Buf (BUF (–) C) (P/N 09587373001)	Tris buffer, EDTA, 0.05% Sodium azide, < 0.01% Poly rA RNA (synthetic)	3 X 0.3 mL	N/A

[a]Product safety labeling follows EU GHS guidance and US FDA regulations.

Table 3: Materials provided

P/N	Material description	Quantity	Storage temperature	Storage time
09731261190	**cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test	20 tests	2-8°C*	Stable until expiration date indicated
09731270190	**cobas® liat** SARS-CoV-2, Influenza A/B & RSV control kit	3 sets	2-8°C	Stable until expiration date indicated

Note: Do not freeze reagents.

*For short-term storage, **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube kits may be stored for up to five days at room temperature. Kits should be labeled with the start date of room temperature storage and disposed of if not used within five days. The **cobas® liat** transfer pipette pack may be stored at room temperature following first removal from the kit.

Table 4: Materials required but not provided

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
Anterior 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
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% Physiological saline*. Thomas Scientific MANTACC™ 0.9% Saline Solution, 3 mL.	20A00K984

*Anterior nasal and nasopharyngeal swabs collected in 0.9% physiological saline solution, Remel™ M4RT, M4, M5 and M6 are compatible for use with **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test. However, clinical performance of the assay in these media types was not established.

Table 5: Equipment and software required but not provided

Equipment and Software
cobas® liat analyzer (P/N 07341920190) Including **cobas® liat** system software version 3.4 or higher
cobas® liat SARS-CoV-2, Influenza A/B & RSV script (CFRA) v1.0.11 or higher

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

Test procedure

Procedural notes

- Do not use **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tube and **cobas® liat** SARS-CoV-2, Influenza A/B & RSV control kit after their expiry dates.
- Do not open individual assay tube packaging until operator is ready to perform testing.
- Do not reuse assay tubes and transfer pipettes. They are for single use only.
- Positive and negative controls contain sufficient volume for single use only. Discard after use.
- Do not use a damaged **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tube. Do not use a **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tube that has been dropped after removal from its foil pouch.
- Ensure there is no sign of leakage from the collection tube prior to running the test.
- Ensure any additional labels are only placed on the back of the tube sleeve or around the side of the cap, do not place labels over barcodes or over the top of the assay tube cap.
- Do not open the cap of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tube during or after the run.
- Dispose of all materials that have come in contact with samples and reagents in accordance with country, state, and local regulations.

Procedural limitations

- **cobas® liat** SARS-CoV-2, Influenza A/B & RSV has been evaluated only for use in combination with the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV control kit and this Instructions for Use document. Modifications to these procedures may alter the performance of the test.
- This test can be used for the detection of SARS-CoV-2, influenza A, influenza B, and/or RSV RNA in nasopharyngeal and nasal swab samples collected in the collection media listed in Table 4. Testing of other sample or media types may lead to inaccurate results.
- Anterior nasal and nasopharyngeal swabs collected in 0.9% physiological saline solution, Remel™ M4RT, M4, M5 and M6 are compatible for use with the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test. Performance of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test with specimens collected in 0.9% physiological saline, Remel™ M4RT, M4, M5 and M6 has been established in analytical studies, however, clinical performance of the assay for these media types was not established.
- Negative results do not preclude SARS-CoV-2, Influenza A, Influenza B, or RSV infection and should not be used as the sole basis for treatment or other patient management decisions.
- This test cannot rule out diseases caused by other bacterial or viral pathogens.
- 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. False negative or invalid results may also occur due to interference. The Internal Control is included in **cobas® liat** SARS-CoV-2, Influenza A/B & RSV to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- 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® liat** SARS-CoV-2, Influenza A/B & RSV could affect primer and/or probe binding that results in failure to detect the presence of virus.

- The performance of this device has not been evaluated for patients receiving intranasally administered influenza vaccine (e.g., FluMist®); **cobas® liat** SARS-CoV-2, Influenza A/B & RSV may detect the agents in those vaccines which may not represent infection by those viruses.
- **cobas® liat** SARS-CoV-2, Influenza A/B & RSV test has not been validated for the testing of pooled specimens or the screening of specimens from asymptomatic individuals.
- Performance characteristics have been determined with specimens from human patients with signs and symptoms of respiratory infection. Performance has not been established for specimens collected from individuals not identified in the intended use population.
- This test does not differentiate influenza A subtypes (i.e., H1N1, H3N2); additional testing is required to differentiate any specific influenza A subtypes or strains, in consultation with local public health departments.
- The 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 clinical evaluation. The evaluation was conducted during September 2023 through March 2024 in the United States. 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. Additional testing with a molecular test and/or sequencing should be considered in situations where a new virus strain or variant is suspected.
- Performance characteristics for influenza A were established during the 2023-2024 season when influenza A/H1N1pdm09 and A/H3N2 were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may differ.
- Positive and negative predictive values are highly dependent on prevalence. The likelihood of a negative result being false is higher during peak activity when prevalence of disease is high. The likelihood of a positive result being false is higher during periods when prevalence is moderate to low.

cobas® liat SARS-CoV-2, Influenza A/B & RSV assay tube Lot Validation

Before using a new lot of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tubes, a Lot Validation procedure must be performed on the **cobas® liat** analyzer to validate the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV 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

From **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test:	From **cobas® liat** SARS-CoV-2, Influenza A/B & RSV control kit:
□ 2 **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tubes □ 2 transfer pipettes □ package insert barcode card	□ 1 negative control (NEG BUF) tube □ 1 **cobas® liat** SARS-CoV-2, Influenza A/B & RSV positive control tube □ 1 negative/positive control barcode card*

*Note: The negative and positive control barcodes for **cobas® liat** SARS-CoV-2, Influenza A/B & RSV are in Section 1 of the control barcode card.

Assay tube Lot Validation workflow

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

cobas® liat SARS-CoV-2, Influenza A/B & RSV sample testing workflow

Material needed for a sample run

- □ 1 **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tube
- □ 1 transfer pipette
- □ 1 sample in appropriate collection media tube

Sample testing workflow

1	Press the power on/off button to start the **cobas® liat** analyzer.
2	Choose **"Logon**". Enter user name and password when prompted, choose **"Enter"**.
3	Obtain clinical sample, **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay tube, and one of the transfer pipettes provided in the **cobas® liat** transfer pipette pack.

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

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

Note: When performing additional positive control and/or negative control runs (with materials provided in the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV control kit), in accordance with local, state, federal and/or accrediting organization requirements, follow the procedures outlined under the section "**cobas® liat** SARS-CoV-2, Influenza A/B & RSV sample testing workflow". In step 5, be sure to use the provided control barcodes (Section 1) included in **cobas® liat** SARS-CoV-2, Influenza A/B & RSV control kit to scan as sample ID barcode. Interpretation of results for **cobas® liat** SARS-CoV-2, Influenza A/B & RSV when running additional **cobas® liat** SARS-CoV-2, Influenza A/B & RSV positive controls or negative controls are shown in the "Interpretation of results" section (Table 6). Using barcodes other than the control barcodes provided may lead to incorrect control results.

Interpretation of results

Table 6: Interpretation of results of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV when running "Lot Validation" procedure or additional control runs

cobas® liat analyzer Display	Result Interpretation
Negative Control Valid	**Negative Control Valid** Control is negative for the presence of SARS-CoV-2, influenza A, influenza B, and RSV RNA.
Negative Control Invalid. Repeat Run	**Negative Control Invalid** Result is Invalid. The negative control should be re-tested to obtain a valid result. Repeat Run.*
Positive Control Valid	**Positive Control Valid** Control is positive for the presence of SARS-CoV-2, influenza A, influenza B, and RSV RNA.
Positive Control Invalid. Repeat Run	**Positive Control Invalid** Result is Invalid. The Positive Control should be re-tested to obtain a valid result. Repeat Run.*

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

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

Table 7: Interpretation of results of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV when running a sample

cobas® liat analyzer Display	Result Interpretation
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).
SARS-CoV-2 Invalid	Presence or absence of SARS-CoV-2 could not be determined. If clinically indicated, repeat assay with same sample or, if possible, collect new sample for testing.
Influenza A Not Detected	Negative test for influenza A (no influenza A RNA detected).
Influenza A Detected	Positive test for influenza A (influenza A RNA present).
Influenza A Invalid	Presence or absence of influenza A could not be determined. If clinically indicated, repeat assay with same sample or, if possible, collect new sample for testing.
Influenza B Not Detected	Negative test for influenza B (no influenza B RNA detected).
Influenza B Detected	Positive test for influenza B (influenza B RNA present).
Influenza B Invalid	Presence or absence of influenza B could not be determined. If clinically indicated, repeat assay with same sample or, if possible, collect new sample for testing.
RSV Not Detected	Negative test for RSV (no RSV RNA detected).
RSV Detected	Positive test for RSV (RSV RNA present).
RSV Invalid	Presence or absence of RSV could not be determined. If clinically indicated, repeat assay with same sample or, if possible, collect new sample for testing.
Assay Invalid	Presence or absence of SARS-CoV-2, influenza A, influenza B, and RSV could not 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.

Non-clinical performance evaluation

Analytical sensitivity (Limit of Detection)

Limit of detection (LoD) studies determine the lowest detectable concentration of SARS-CoV-2, influenza A, influenza B, and RSV at which equal to or greater than 95% of all replicates test positive.

Two strains for each target (SARS-CoV-2, influenza A, influenza B, and RSV) were evaluated. To determine the LoD for each target, co-spiked panels were formulated using cultured or inactivated viral material diluted in pooled negative nasopharyngeal swab matrix. Twenty-one replicates per lot of assay tubes per dilution were tested for five or six 2-fold dilutions using three lots of assay tubes. The strains evaluated, as well as their corresponding LoD values are shown in Table 8.

Table 8: LoD determination for SARS-CoV-2, influenza A, influenza B, and RSV strains

Virus	Strain	Concentration at LoD	Hit rate (Mean Ct)
SARS-CoV-2*	USA-WA1/2020	0.0350 $TCID_{50}$/mL	20/21 (35.5)
SARS-CoV-2*	WHO International Standard 20/146, v3, 11/2021	65.1 IU/mL	21/21 (34.9)
Influenza A	Darwin/6/2021	0.295 $TCID_{50}$/mL	21/21 (35.0)
Influenza A	Brisbane/02/2018	0.00325 $TCID_{50}$/mL	21/21 (36.4)
Influenza B	B/Austria/1359417/2021	0.979 $TCID_{50}$/mL	20/21 (34.6)
Influenza B	Phuket/3073/2013	0.183 $TCID_{50}$/mL	21/21 (34.1)
RSV	9320 (Subtype B)	0.269 $TCID_{50}$/mL	21/21 (34.9)
RSV	Long (Subtype A)	0.0240 $TCID_{50}$/mL	21/21 (33.8)

*Inactivated virus

A separate study was performed to demonstrate that the LoD of each strain individually was equivalent to the co-spiked LoD.

Reactivity/inclusivity

The inclusivity study evaluates the ability of the test to detect SARS-CoV-2, influenza A influenza B, and RSV isolates/variants. The reactivity/inclusivity was evaluated with 10 SARS-CoV-2, 28 influenza A (15 H1N1, 10 H3N2, 1 H5N1, 1 H5N2, & 1 H7N9), ten (10) influenza B (5 Victoria and 5 Yamagata), and five (5) RSV isolates/variants. All strains were individually tested at ~3x LoD in 3 replicates to evaluate inclusivity. If < 100% hit rate was observed, the concentration was doubled until 3/3 replicates were detected.

SARS-CoV-2

The SARS-CoV-2 isolates/variants were tested as inactivated viruses in the study and the lowest concentrations detected are listed in Table 9.

In silico analysis on January 15, 2025 indicates 99.9% detection of all available SARS-CoV-2 sequences in the GISAID (>7.94M sequences) and NCBI (>15.04M sequences) databases.

Table 9: Results of Testing SARS-CoV-2 Isolate/Variants

Lineage/Subtype	Isolate/Variant*	Test Concentration ($TCID_{50}$/mL)	Relative to LoD
Alpha	Hong Kong/VM20001061/2020	0.105	3x
Beta, B.1.595_2020 (was B.1.2)	NY-Wadsworth-33126-01/2020	0.105	3x
Delta, B.1.617.2	USA/MD-HP05285/2021	0.105	3x
Epsilon, B.1.427	USA/CA/VRLC009/2021	0.105	3x
Gamma, P.1	Japan/TY7-503/2021	0.105	3x
Iota, B.1.526_2021	USA/NY-Wadsworth-21025952-01/2021	0.105	3x

Lineage/Subtype	Isolate/Variant*	Test Concentration ($TCID_{50}$/mL)	Relative to LoD
Kappa, B.1.617.1	USA/CA-Stanford-15_S02/2021	0.105	3x
Omicron, B.1.1.529, CH.1.1	USA/MD-HP41275/2022	0.105	3x
Omicron, B.1.1.529, XBB.1.5	USA/MD-HP40900/2022	0.105	3x
Zeta, P2_2021	USA/NY-Wadsworth-21006055-01/2021	0.105	3x

*These strains are in addition to the SARS-CoV-2 USA-WA1/2020 and WHO Standard 20/146, v3, 11/2021 used in the analytical sensitivity study.

Influenza A

The influenza A isolates/variants tested in the study and the lowest concentrations detected are listed in Table 10.

Table 10: Results of Testing Influenza A Isolate/Variants

Lineage/Subtype	Isolate/Variant*	Test Concentration ($TCID_{50}$/mL)[a]	Relative to LoD
H1N1	A/Brisbane/59/07	0.885	3x
H1N1	A/Christ Church/16/2020	1.77 EID_{50}/mL	6x
H1N1	A/Denver/01/57	0.885	3x
H1N1	A/England/221740513/2022**	75 copies/mL‡	1x
H1N1	A/England/224020815/2022**	91.5 copies/mL‡	1x
H1N1	A/Fort Monmouth/01/47	0.885	3x
H1N1	A/Malaya/302/54	0.885	3x
H1N1	A/New Caledonia/20/99	0.885	3x
H1N1	A/Swine/Iowa/15/30	1.77 $CEID_{50}$/mL	6x
H1N1	A/Sydney/5/2021β	1.77	6x
H1N1	A/Victoria/2570/2019	3.54 EID_{50}/mL	12x
H1N1	A/WS/33	0.885	3x
H1N1	A/Brisbane/14/2023	75 copies/mL‡	1x
H1N1	A/Townsville/1A/2023	75 copies/mL‡	1x
H1N1	A/ Townsville/2A/2023	75 copies/mL‡	1x
H3N2	A/Aichi/2/68	0.885 $CEID_{50}$/mL	3x
H3N2	A/Brisbane/10/07	0.885	3x
H3N2	A/Cambodia/E0826360/2020	0.885	3x
H3N2	A/Darwin/9/2021	1.77	6x
H3N2	A/Hong Kong/8/68	0.885	3x
H3N2	A/H3/Perth/16/09	0.885	3x
H3N2	A/Tasmania/503/2020	0.885 EID_{50}/mL	3x
H3N2	A/Victoria/3/75	0.885 $CEID_{50}$/mL	3x
H3N2	A/Wisconsin/67/2005	0.885	3x
H3N2	A/Singapore/INFIMH-16-0019/2016	0.885	3x
H5N1	A/mallard/Wisconsin/2576/2009	0.885 $CEID_{50}$/mL	3x
H5N2	A/ruddy turnstone/New Jersey/828212/2001	0.885 $CEID_{50}$/mL	3x
H7N9	A/northern shoveler/Mississippi/11OS145/2011	3.54 $CEID_{50}$/mL	12x

*These strains are in addition to the influenza A Darwin/6/2021 and Brisbane/02/2018 strains used in the analytical sensitivity study.

**A/England/221740513/2022 GISAID ID is EPI_ISL_14387941 and for A/England/224020815/2022 GISAID ID is EPI_ISL_15803829.

[‡] The concentrations tested are near the 1x LOD value (69 copies/mL) determined by digital PCR for the influenza A/Darwin/6/2021 strain in Table 8.
[ä] Concentrations are shown in $TCID_{50}$/mL unless otherwise indicated.
[β] Inactivated virus

Influenza B

The influenza B isolates/variants tested in the study and the lowest concentrations detected are listed in Table 11.

Table 11: Results of Testing Influenza B Isolate/Variants

Lineage/Subtype	Isolate/Variant*	Test Concentration($TCID_{50}$/mL)[ä]	Relative to LoD
Victoria	B/Brisbane/60/2008	2.937	3x
Victoria	B/Colorado/06/2017	2.937	3x
Victoria	B/Malaysia/2506/04	2.937	3x
Victoria	B/Michigan/09/2011	2.937 EID_{50}/mL	3x
Victoria	B/Washington/02/2019	2.937	3x
Yamagata	B/Florida/04/06	2.937	3x
Yamagata	B/Massachusetts/2/2012	2.937	3x
Yamagata	B/Texas/6/2011	2.937	3x
Yamagata	B/Texas/81/2016	2.937 EID_{50}/mL	3x
Yamagata	B/Wisconsin/1/2010	2.937	3x

*These strains are in addition to the influenza B Austria/1359417/2021 and Phuket/3073/2013 strains used in the analytical sensitivity study.
[ä] Concentrations are shown in $TCID_{50}$/mL unless otherwise indicated.

RSV

The RSV isolates/variants tested in the study and the lowest concentrations detected are listed in Table 12.

Table 12: Results of Testing RSV Isolate/Variants

Lineage/Subtype	Isolate/Variant*	Test Concentration ($TCID_{50}$/mL)	Relative to LoD
RSV-A	RSV-A 2006 isolate	0.807	3x
RSV-A	RSV-A2	0.807	3x
RSV-B	RSV-B Ch93(18)-18	0.807	3x
RSV-B	RSV-B Wash/18537/62	0.807	3x
RSV-B	RSV-B WV/14617/85	0.807	3x

*These strains are in addition to the RSV 9320 (Subtype B) and Long (Subtype A) strains used in the analytical sensitivity study.

Cross reactivity and microbial interference

Cross-reactivity and microbial interference were evaluated by testing a panel of microorganisms (Table 13). High titer stocks of the potentially cross-reacting microorganisms were tested for cross-reactivity, and also in the presence of SARS-CoV-2, influenza A, influenza B, and RSV at 3x LoD concentrations for microbial interference. Three (3) replicates in target negative background and three (3) replicates in target positive background were tested for each non-target microorganism. The testing concentrations for potentially interfering viruses are ≥1.0E+05 units/mL except for three viruses (SARS Coronavirus, Urbani, Human Rhinovirus Type 1A, and Human Parainfluenza Virus Type 4A) which were tested at a concentration less than 1.0e+5, but higher than 1.0e+4 units/mL due to their low stock concentration. Other microorganisms (non-virus) were tested at ≥1.0E+06 units/mL. Clinical specimens containing Human Coronavirus

HKU1 and *Pneumocystis jirovecii* were also tested (concentrations were unknown). None of the organisms tested cross reacted or interfered with **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test performance at the concentrations tested.

Table 13: Microorganisms tested for cross-reactivity and microbial interference

Adenovirus Type 1[β]	Human Rhinovirus B	*Mycobacterium tuberculosis*
Adenovirus Type 7	MERS-Coronavirus[β]	*Mycoplasma genitalium*[β]
Cytomegalovirus	Measles	*Mycoplasma pneumoniae*
Epstein-Barr virus[β]	Mumps	*Neisseria elongata*
Human Coronavirus OC43	SARS Coronavirus, Urbani*[β]	*Neisseria flava*
Human Coronavirus 229E	*Bordetella parapertussis*	*Neisseria meningitidis*
Human Coronavirus HKU[ł]	*Bordetella pertussis*	*Pneumocystis jirovecii*[ł]
Human Coronavirus NL63[β]	*Chlamydophila pneumoniae*	*Pseudomonas aeruginosa*
Human Enterovirus 68	*Corynebacterium flavescens*	*Staphylococcus aureus*
Human Metapneumovirus 27	*Escherichia coli*	*Staphylococcus epidermidis*
Human Parainfluenza Virus Type 1[β]	*Fusobacterium necrophorum subsp. necrophorum*	*Streptococcus pneumoniae*
Human Parainfluenza Virus Type 2	*Haemophilus influenzae*	*Streptococcus pyogenes*
Human Parainfluenza Virus Type 3	*Lactobacillus crispatus*	*Streptococcus salivarius*
Human Parainfluenza Virus Type 4A*[β]	*Legionella pneumophila*	*Aspergillus flavus var. flavus*
Human Rhinovirus Type 1A*[β]	*Moraxella catarrhalis*	*Candida albicans*

* Tested at highest concentration available

[β] Inactivated virus

[ł] Clinical specimens at unknown concentrations were tested.

Competitive inhibition

To assess competitive inhibition between SARS-CoV-2, influenza A, influenza B, and RSV, each target prepared at high concentrations with the other three targets at low concentrations (approximately three times the respective LoD) was tested to evaluate any potential impact by the high concentration target on the detection of the other targets (Table 14). Five (5) replicates were tested for each concentration combination.

Testing results indicated that when one viral target was present at high concentrations tested, no interference was observed for the other three viral targets that were present at low concentrations (~3x LoD).

Table 14: Competitive inhibition strains and concentrations tested with the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test

Assay Target	Strain	3x LoD Concentration ($TCID_{50}$/mL)	High Concentration Used in Combination with other Low Concentration Targets ($TCID_{50}$/mL)
SARS-CoV-2*	SARS WA 1/2020	0.105	1.14E+05
Influenza A	A/Darwin/6/2021	0.885	1.48E+06
Influenza B	B/Austria/1359417/2021	2.937	9.79E+06
RSV	RSV 9320	0.807	1.35E+06

* Inactivated virus

Endogenous and exogenous interference

Potentially interfering substances that may be commonly encountered in respiratory specimens were evaluated. Each substance was tested, by introducing potential interferents. Five (5) replicates were tested with and five (5) replicates were tested without 3x LoD SARS-CoV-2, influenza A, influenza B, and RSV targets. The substances listed in Table 15 at the concentrations tested did not interfere in the detection of SARS-CoV-2, influenza A, influenza B or RSV nor did they produce invalid results in negative samples.

Table 15: Endogenous and Exogenous Interference

Potential Interferent	Concentration Tested
Peripheral blood mononuclear cell (PBMC)	1.00E+06 cell/mL
Mucin: bovine submaxillary gland, type I-S	5 mg/mL
Human Whole Blood	5% v/v
Nasal spray - Afrin / Anefrin	15% v/v
Nasal corticosteroids - Flonase	5% (v/v)
Nasal gel - Zicam	5% (v/v)
Throat lozenges, oral anesthetic and analgesic – Cepacol**	5 mg/mL
Antibiotic, nasal ointment - Bactroban mupirocin ointment	5 mg/mL
Antiviral drug – Relenza	5 mg/mL
Antiviral drug - Tamiflu	7.5 mg/mL
Antimicrobial, systemic- Tobramycin	4 µg/mL
Intranasal Vaccine – FluMist*	6.25% (v/v)

*FluMist® contains influenza A and B virus and will test positive if present in the sample. See Procedural limitations.

** One invalid result was obtained in the presence of target analytes. Repeat testing was performed and all targets were detected. The one invalid result was most likely caused by other factors such as general tube processing error, lot variation, etc. that are not related to the interference test condition.

Reproducibility study

A reproducibility study assessed the total variability of the assay in detecting SARS-CoV-2, influenza A, influenza B, and RSV across operators, study sites, testing days, analyzers, and assay tube lots. The reproducibility was evaluated at three (3) study sites representative of intended use settings. Two (2) operators at each of the three (3) sites tested a 3-member reproducibility panel in triplicate on five (5) different days for three (3) assay tube lots. The reproducibility panel comprises a low positive (1-2x LoD) and a moderate positive (3-5x LoD) co-formulated for SARS-CoV-2, influenza A, influenza B, and RSV, in addition to negative samples. The expected result for the true negative panel member is "Not Detected," while the expected result for the low positive and moderate positive panel members is "Detected." Percent agreement with expected result is shown in Table 16.

Table 16: Reproducibility results for **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test

Target Analyte	Expected Panel Member Concentration	Valid Tests (N)	Results in Agreement with Target Analyte (n)	Percent Agreement n/N x 100	95% Score CI
Negative	0	265	265	100.0	(98.6, 100.0)
SARS-CoV-2	1x-2x LoD	270	270	100.0	(98.6, 100.0)
SARS-CoV-2	3x-5x LoD	267	267	100.0	(98.6, 100.0)
Influenza A	1x-2x LoD	269	268	99.6	(97.9, 99.9)
Influenza A	3x-5x LoD	267	267	100.0	(98.6, 100.0)
Influenza B	1x-2x LoD	269	268	99.6	(97.9, 99.9)
Influenza B	3x-5x LoD	267	267	100.0	(98.6, 100.0)
RSV	1x-2x LoD	270	270	100.0	(98.6, 100.0)
RSV	3x-5x LoD	267	267	100.0	(98.6, 100.0)

Note: Results were in agreement when a positive panel member had a valid result of "Detected" for the analyte or when the negative panel member had a valid result of "Not Detected" for the analyte.

The means, standard deviations, and coefficients of variation (%) for cycle threshold (Ct) values by target analyte and expected concentration (Positive Panel Members) are shown in Table 17.

Table 17: Overall Mean Estimate, Standard Deviations, and Coefficients of Variation (%) for Cycle Threshold Values by Target Analyte and Expected Concentration (Positive Panel Members) for the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test.

Target Analyte	Expected Concen-tration	n/N[a]	Mean Ct	Site SD	Site CV%	Lot SD	Lot CV%	Day SD	Day CV%	Run SD[b]	Run CV%	Within-Run (Residual) SD	Within-Run (Residual) CV%	Total SD	Total CV%
SARS-CoV-2	1x-2x LoD	270/270	33.8	0.00	0.0	0.38	1.1	0.17	0.5	0.36	1.1	1.03	3.0	1.16	3.4
SARS-CoV-2	3x-5x LoD	267/267	32.4	0.13	0.4	0.54	1.7	0.27	0.8	0.00	0.0	1.00	3.1	1.18	3.6
Influenza A	1x-2x LoD	268/269	34.8	0.11	0.3	0.08	0.2	0.13	0.4	0.00	0.0	0.62	1.8	0.65	1.9
Influenza A	3x-5x LoD	267/267	33.8	0.00	0.0	0.05	0.2	0.00	0.0	0.11	0.3	0.39	1.2	0.41	1.2
Influenza B	1x-2x LoD	268/269	33.8	0.04	0.1	0.29	0.9	0.00	0.0	0.13	0.4	0.66	2.0	0.73	2.2
Influenza B	3x-5x LoD	267/267	32.8	0.05	0.2	0.47	1.4	0.12	0.4	0.00	0.0	0.52	1.6	0.71	2.2
RSV	1x-2x LoD	270/270	34.3	0.00	0.0	0.19	0.5	0.07	0.2	0.00	0.0	0.82	2.4	0.84	2.5
RSV	3x-5x LoD	267/267	33.0	0.06	0.2	0.17	0.5	0.00	0.0	0.14	0.4	0.69	2.1	0.73	2.2

Note: Ct = cycle threshold; LoD = Limit of Detection; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus-2; RSV = Respiratory syncytial virus; SD = standard deviation; CV% = percent coefficient of variation.

[a] n is the number of positive tests, which contribute Ct values to the analysis. N is the total number of valid tests for the panel member by target analyte.

[b] In the reproducibility study, each panel member was tested in triplicate, defining one run.

Clinical performance evaluation

Prospective Study

The clinical performance of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV for the detection of SARS-CoV-2, influenza A, influenza B, and RSV was evaluated using paired prospective fresh nasopharyngeal swab (NPS) and anterior nasal swab (ANS) specimens collected in Universal Viral Transport medium (UVT) or Universal Transport Medium (UTM) from individuals with signs and symptoms of respiratory viral infection. For prospectively enrolled subjects an NPS specimen was collected from each subject along with either a self-collected or a healthcare-provider collected ANS specimen. Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) were determined by comparing the results of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV to the results of an FDA-cleared Nucleic Acid Amplification Test (NAAT).

Prospective clinical (Category I) specimens were collected and tested in a non-interventional study between September 2023 and March 2024 at 14 point of care testing sites in the United States (US). Of the 1729 prospective symptomatic subjects enrolled, 1704 NPS specimens were evaluable in the SARS-CoV-2, influenza A, and influenza B analyses, 20 were non-evaluable due to missing or invalid **cobas® liat** test results, and 5 were non-evaluable due to specimen handling issues. 1705 NPS specimens were evaluable in the RSV analyses, 19 were non-evaluable due to missing or invalid **cobas® liat** test results, and 5 were non-evaluable due to specimen handling issues. Of the 1729 prospective symptomatic subjects enrolled, 1705 ANS specimens were evaluable in the SARS-CoV-2 and influenza B analyses, 23 were non-evaluable due to missing or invalid **cobas® liat** test results, and 1 was non-evaluable due to specimen handling issues. Two (2) additional ANS specimens obtained inconclusive comparator results for influenza A, leaving 1703 ANS specimens in the influenza A analysis. 1706 ANS specimens were evaluable in the RSV analyses, 22 were non-evaluable due to missing or invalid **cobas® liat** test results, and 1

was non-evaluable due to specimen handling issues. Available demographic data regarding the individuals from whom specimens were obtained are presented in Table 18.

Table 18: Demographics of Prospectively Enrolled Individuals

Characteristics	Overall N(%) (N=1729)
Sex at Birth	-
Male	681 (39.4%)
Female	1048 (60.6%)
Age Group (Years)	-
<1	33 (1.9%)
1 - <18	434 (25.1%)
18 - <30	381 (22.0%)
30 - <40	246 (14.2%)
40 - <50	200 (11.6%)
50 - <60	181 (10.5%)
>=60	254 (14.7%)
Ethnicity	-
Hispanic / Latino	244 (14.1%)
Not Hispanic / Latino	1478 (85.5%)
Not Reported	4 (0.2%)
Unknown	3 (0.2%)
Race	-
American Indian / Alaska Native	8 (0.5%)
Asian	24 (1.4%)
Black / African American	212 (12.3%)
Native Hawaiian / Other Pacific Islander	3 (0.2%)
White	1413 (81.7%)
Other Race	52 (3.0%)
Not Reported	17 (1.0%)

For the NPS specimens, **cobas® liat** SARS-CoV-2, Influenza A/B & RSV demonstrated a PPA and NPA of 94.5% and 97.6% for SARS-CoV-2, respectively; 100.0% and 99.3% for influenza A, respectively; 100.0% and 99.3% for influenza B, respectively; and 100.0% and 99.0% for RSV, respectively (Table 19). For the ANS specimens, **cobas® liat** SARS-CoV-2, Influenza A/B & RSV demonstrated a PPA and NPA of 96.7% and 97.2% for SARS-CoV-2, respectively; 100.0% and 99.3% for influenza A, respectively; 100.0% and 99.5% for influenza B, respectively; and 97.5% and 98.8% for RSV, respectively (Table 19). The initial invalid rate of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV on NPS and ANS specimens was 0.5% and 0.7% respectively. Upon repeat testing, the final assay invalid rate on NPS and ANS was 0% and 0.1% respectively.

Table 19: Clinical Performance of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV relative to the comparator by Specimen Type and Target

Target	Specimen Type	a/(a+c)	PPA (%)	PPA 95% CI	d/(b+d)	NPA (%)	NPA 95% CI
SARS-CoV-2*	NPS	207/219	94.5	90.7-96.8	1450/1485	97.6	96.7-98.3
SARS-CoV-2**	ANS	208/215	96.7	93.4-98.4	1448/1490	97.2	96.2-97.9
Influenza A#	NPS	54/54	100.0	93.4-100.0	1639/1650	99.3	98.8-99.6
Influenza A##	ANS	53/53	100.0	93.2-100.0	1639/1650	99.3	98.8-99.6
Influenza B&	NPS	22/22	100.0	85.1-100.0	1670/1682	99.3	98.8-99.6

Influenza B[&&]	ANS	24/24	100.0	86.2-100.0	1672/1681	99.5	99.0-99.7
RSV[$]	NPS	70/70	100.0	94.8-100.0	1618/1635	99.0	98.3-99.3
RSV[$$]	ANS	79/81	97.5	91.4-99.3	1606/1625	98.8	98.2-99.3

Abbreviations: PPA = Positive Percent Agreement; CI = Score Confidence Interval; NPA = Negative Percent Agreement; NPS = Nasopharyngeal swab; ANS = Anterior nasal swab; RSV=Respiratory syncytial virus; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2.

Note: N = Total number of specimens; a = number of specimens where both **cobas® liat** and the comparator are positive; b = number of specimens where **cobas® liat** is positive and the comparator is negative; c = number of specimens where **cobas® liat** is negative and the comparator is positive; d = number of specimens where both **cobas® liat** and the comparator are negative.

[*] SARS-CoV-2 NPS discrepant NAAT results: Of 12 specimens negative on **cobas® liat** and positive on the comparator, 8 were positive and 4 were negative. Of 35 specimens positive on **cobas® liat** and negative on the comparator, 12 were positive and 23 were negative .

[#] Influenza A NPS discrepant NAAT results: Of 11 specimens positive on **cobas® liat** and negative on the comparator, 2 were positive and 9 were negative.

[&] Influenza B NPS discrepant NAAT results: Of 12 specimens positive on **cobas® liat** and negative on the comparator, all 12 were negative.

[$] RSV NPS discrepant NAAT results: Of 17 specimens positive on **cobas® liat** and negative on the comparator, 2 were positive and15 were negative.

[**] SARS-CoV-2 ANS discrepant NAAT results: Of 7 specimens negative on **cobas® liat** and positive on the comparator, 6 were positive and 1 was negative. Of 42 specimens positive on **cobas® liat** and negative on the comparator, 8 were positive and 34 were negative.

[##] Influenza A ANS discrepant NAAT results: Of 11 specimens positive on **cobas® liat** and negative on the comparator, 1 was positive and 10 were negative.

[&&] Influenza B ANS discrepant NAAT results: Of 9 specimens positive on **cobas® liat** and negative on the comparator, all 9 were negative.

[$$] RSV ANS discrepant NAAT results: Of 2 specimens negative on **cobas® liat** and positive on the comparator, 1 was positive and 1 was negative. Of 19 specimens positive on **cobas® liat** and negative on the comparator, all 19 specimens were negative.

Retrospective Study

Influenza B was of lower prevalence and was not encountered in sufficiently large numbers during the prospective clinical study to adequately demonstrate assay performance. To supplement the results of the prospective clinical study, retrospective frozen clinical NPS and ANS specimens collected in Universal Viral Transport medium (UVT) or Universal Transport Medium (UTM) from individuals with signs and symptoms of respiratory viral infection were tested. Frozen archived (Category III) influenza B positive and negative NPS (n=223) and ANS (n=206) specimens obtained between 2019 and 2023 were distributed to 6 sites and tested in the course of the daily workflow. One NPS sample pre-characterized as positive for influenza B was non-evaluable due to missing/invalid results on the comparator method. The comparator method was an acceptable FDA-cleared molecular assay. Available demographic data regarding the individuals from the retrospective study are shown in Table 20.

Table 20: Demographics of Subjects from Retrospective Population

Characteristics	**Overall N(%) (N=429)**
Sex at Birth	**-**
Male	151 (35.20%)
Female	226 (52.68%)
Not Reported	52 (12.12%)
Age Group (Years)	**-**
<1	0 (0.00%)
1 - <18	129 (30.07%)
18 - <30	77 (17.95%)
30 - <40	79 (18.41%)

Characteristics	Overall N(%) (N=429)
40 - <50	28 (6.53%)
50 - <60	14 (3.26%)
>=60	23 (5.36%)
Not Reported	79 (18.41%)
Ethnicity	-
Hispanic / Latino	98 (22.84%)
Not Hispanic / Latino	112 (26.11%)
Not Reported	213 (49.65%)
Other	5 (1.17%)
Unknown	1 (0.23%)
Race	-
American Indian / Alaska Native	2 (0.47%)
Asian	3 (0.70%)
Black / African American	12 (2.80%)
White	196 (45.69%)
Other Race	3 (0.70%)
Unknown	5 (1.17%)
Not Reported	208 (48.48%)

For the retrospective NPS specimens, **cobas® liat** SARS-CoV-2, Influenza A/B & RSV demonstrated a PPA and NPA of 100.0% and 97.9% for influenza B, respectively (Table 21). For the retrospective ANS specimens, **cobas® liat** SARS-CoV-2, Influenza A/B & RSV demonstrated a PPA and NPA of 100.0% and 98.3% for influenza B, respectively (Table 21). No invalid results were observed for the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV with retrospective NPS or ANS specimens for an invalid rate of 0.0%.

Table 21: Agreement of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test and Comparator Test for influenza B in Retrospective Samples

Target	Specimen Type	a/(a+c)	PPA (%)	PPA 95% CI	d/(b+d)	NPA (%)	NPA 95% CI
Influenza B*	NPS	34/34	100.0	89.8-100.0	184/188	97.9	94.7-99.2
Influenza B**	ANS	34/34	100.0	89.8-100.0	169/172	98.3	95.0-99.4

Abbreviations: PPA = Positive Percent Agreement; CI = Score Confidence Interval; NPA = Negative Percent Agreement; NPS = Nasopharyngeal swab; ANS = Anterior nasal swab; RSV=Respiratory syncytial virus; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2.

Note: N = Total number of specimens; a = number of specimens where both **cobas® liat** and the comparator are positive; b = number of specimens where **cobas® liat** is positive and the comparator is negative; c = number of specimens where **cobas® liat** is negative and the comparator is positive; d = number of specimens where both **cobas® liat** and the comparator are negative.

* Influenza B NPS discrepant NAAT results: Of 4 specimens positive on **cobas® liat** and negative on the comparator, all 4 were negative.

** Influenza B ANS discrepant NAAT results: Of 3 specimens positive on **cobas® liat** and negative on the comparator, 1 was positive and 2 were negative.

Expected values

The positivity rate of the **cobas® liat** SARS-CoV-2, Influenza A/B, and RSV nucleic acid assay test for each target observed during the prospective study is shown for each specimen type, by collection site in Table 22 below.

Table 22: Positivity as Determined by the **cobas® liat** SARS-CoV-2, Influenza A/B, and RSV nucleic acid test by Specimen Type and Clinical Site in the Prospective Study

Collection Site	SARS-CoV-2		Influenza A		Influenza B		RSV	
	NPS	ANS	NPS	ANS	NPS	ANS	NPS	ANS
1	6.0% (4/67)	7.5% (5/67)	4.5% (3/67)	4.5% (3/67)	0.0% (0/67)	0.0% (0/67)	0.0% (0/67)	0.0% (0/67)
2	12.2% (5/41)	12.2% (5/41)	2.4% (1/41)	0.0% (0/41)	2.4% (1/41)	2.4% (1/41)	4.9% (2/41)	4.9% (2/41)
3	6.1% (2/33)	3.0% (1/33)	0.0% (0/33)	0.0% (0/33)	0.0% (0/33)	0.0% (0/33)	18.2% (6/33)	18.2% (6/33)
4	0.0% (0/42)	0.0% (0/42)	7.1% (3/42)	9.5% (4/42)	0.0% (0/42)	0.0% (0/42)	19.0% (8/42)	21.4% (9/42)
5	17.5% (54/308)	21.5% (66/307)	0.3% (1/308)	0.0% (0/307)	1.0% (3/308)	0.7% (2/307)	1.6% (5/308)	2.9% (9/307)
6	20.0% (34/170)	20.3% (35/172)	10.0% (17/170)	10.5% 18/172)	0.0% (0/170)	0.0% (0/172)	5.8% (10/171)	4.6% (8/173)
7	7.1% (13/184)	8.1% (15/185)	3.3% (6/184)	3.8% (7/185)	8.7% (16/184)	8.1% 15/185)	18.5% 34/184)	21.6%(40/185)
8	3.0% (2/66)	3.0% (2/66)	1.5% (1/66)	0.0% (0/66)	1.5% (1/66)	1.5% (1/66)	1.5% (1/66)	1.5% (1/66)
9	26.1% (42/161)	26.1% (42/161)	3.1% (5/161)	3.1% (5/161)	2.5% (4/161)	2.5% (4/161)	3.7% (6/161)	3.7% (6/161)
10	17.3% (29/168)	16.7% (28/168)	0.6% (1/168)	0.6% (1/168)	0.0% (0/168)	0.0% (0/168)	1.2% (2/168)	1.2% (2/168)
11	14.5% (29/200)	12.9% (26/201)	1.5% (3/200)	1.0% (2/201)	0.0% (0/200)	0.0% (0/201)	0.0% (0/200)	1.0% (2/201)
12	3.9% (6/154)	3.9% (6/152)	11.0% (17/154)	11.8%(18/152)	1.9% (3/154)	2.6% (4/152)	6.5% (10/154)	6.6% (10/152)
13	14.3% (8/56)	12.5% (7/56)	1.8% (1/56)	0.0% (0/56)	10.7% (6/56)	10.7% (6/56)	3.6% (2/56)	3.6% (2/56)
14	25.9% (14/54)	22.2% (12/54)	11.1% (6/54)	13.0% (7/54)	0.0% (0/54)	0.0% (0/54)	1.9% (1/54)	1.9% (1/54)

Note: NPS = Nasopharyngeal swab; ANS = Anterior nasal swab; RSV=Respiratory syncytial virus; SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2.

Failure codes

The result report may contain failure codes as described in Table 23, depending on potential run failures. For any questions, please contact your Roche Service representative.

Table 23: Failure codes and definitions

Failure Codes	Sample	Negative Control	Positive Control
g0/g1	IC out of range.	IC out of range.	IC out of range.
x4	SARS-CoV-2, influenza A, influenza B, and/or RSV target out of range.	N/A	SARS-CoV-2, influenza A, influenza B, and/or RSV target out of range.
FP	N/A	SARS-CoV-2, influenza A, influenza B, and/or RSV target out of range.	N/A
x5	Low sample volume.	Low sample volume.	N/A

CLIA Waiver Study

Clinical performance characteristics of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV test were evaluated in a multi-site prospective study during September 2023 to March 2024 in the U.S. Fourteen (14) point of care (POC) testing sites throughout the U.S. participated in the clinical study. All the sites qualified as representative of CLIA waived intended use sites for this device.

Operators at all 14 external POC sites were chosen to represent the intended users. From these sites, 41 operators took part in study testing and were chosen to represent typical POC operators (e.g., nurses, medical assistants, clinical research coordinators).

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

Near Cutoff Study

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

Two (2) operators at each of the three (3) sites, each tested one (1) panel on five (5) different days for three (3) assay tube lots. All replicates for each panel member were always tested on the same analyzer. For each panel member, approximately 270 results were produced as described in Table 24.

Table 24: Results for near cutoff study with **cobas® liat** SARS-CoV-2, Influenza A/B & RSV

Target Analyte	Panel Member Concentration	Site 1 Agreement with Expected Results^	Site 2 Agreement with Expected Results^	Site 3 Agreement with Expected Results^	Overall Agreement with Expected Results^
SARS-CoV-2	1x-2x LoD	100.0% (90/90) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (270/270) (98.6%-100.0%)
SARS-CoV-2	Negative	100.0% (86/86) (95.7%-100.0%)	100.0% (89/89) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (265/265) (98.6%-100.0%)
Influenza A	1x-2x LoD	100.0% (90/90) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	98.9 % (88/89) (93.9%- 99.8%)	99.6 % (268/269) (97.9%- 99.9%)
Influenza A	Negative	100.0% (86/86) (95.7%-100.0%)	100.0% (89/89) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (265/265) (98.6%-100.0%)
Influenza B	1x-2x LoD	100.0% (90/90) (95.9%-100.0%)	98.9 % (89/90) (94.0%- 99.8%)	100.0% (89/89) (95.9%-100.0%)	99.6 % (268/269) (97.9%- 99.9%)
Influenza B	Negative	100.0% (86/86) (95.7%-100.0%)	100.0% (89/89) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (265/265) (98.6%-100.0%)
RSV	1x-2x LoD	100.0% (90/90) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (270/270) (98.6%-100.0%)

Target Analyte	Panel Member Concentration	Site 1 Agreement with Expected Results^	Site 2 Agreement with Expected Results^	Site 3 Agreement with Expected Results^	Overall Agreement with Expected Results^
RSV	Negative	100.0% (86/86) (95.7%-100.0%)	100.0% (89/89) (95.9%-100.0%)	100.0% (90/90) (95.9%-100.0%)	100.0% (265/265) (98.6%-100.0%)

Note: LoD: limit of detection.

^Percent Agreement with Expected Results (n/N) (95% Score Confidence Interval)

Flex Studies

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.

Symbols

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

Table 25: 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 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

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