Rx Only

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

For use under Emergency Use Authorization (EUA) only

For in vitro diagnostic use

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

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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) RNA in anterior nasal (nasal) swab and nasopharyngeal swab specimens collected from individuals with signs and symptoms of respiratory tract infection consistent with COVID-19 by their healthcare provider. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2, influenza and RSV can be similar.

Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high, moderate or waived complexity tests. The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Results are for the simultaneous detection and differentiation of SARS-CoV-2, influenza A, influenza B and RSV viral RNA in clinical specimens and are not intended to detect influenza C virus. SARS-CoV-2, influenza A, influenza B and RSV RNA are generally detectable in nasal swab and nasopharyngeal swab specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2, influenza A, influenza B and/or RSV RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other pathogens not detected by the test. The agent detected may not be the definitive cause of disease.

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

The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test is intended for use by trained operators specifically instructed in the use of the **cobas® liat** system and the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test. The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test is only for use under the Food and Drug Administration's Emergency Use Authorization.

Summary

In late 2019, an outbreak of novel coronavirus spread worldwide, prompting the World Health Organization (WHO) to declare a public health emergency of international concern in early 2020.[1,2] Globally, as of October 2023, there have been more than 770 million confirmed cases of coronavirus disease 2019 (COVID-19) including 6.9 million deaths reported to WHO, although actual case numbers are estimated to be higher.[3] The implicated pathogen, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is an enveloped ribonucleic acid virus of zoonotic origin.[4] Coronaviruses (CoVs) are a large family of viruses that are common in many different animal species, including some that are common in humans (e.g., human coronaviruses: 229E, NL63, OC43, and HKU1).[4-6] Animal CoVs rarely infect humans, but when they do, they can cause mild respiratory infection ranging up to more severe disease (e.g., Middle East respiratory syndrome [MERS] and severe acute respiratory syndrome [SARS-CoV]).[4] SARS-CoV-2 most commonly causes fever and respiratory symptoms (e.g., cough and shortness of breath).[7-9] Abdominal pain, diarrhea, vomiting, headache, and myalgia are other possible manifestations. The clinical presentation of COVID-19 can vary from asymptomatic infection or mild illness to fatal

disease.[7-9] It is transmitted directly from person to person primarily via respiratory secretions.[10,11]

Prior to the SARS-CoV-2 pandemic, influenza virus was globally estimated to cause over one billion infections each year, and 290,000-650,000 deaths each year due to associated respiratory diseases.[12,13] Influenza and lower respiratory tract infections are significant causes of worldwide morbidity and mortality.[14-18] The highest burden of disease affects infants and young children, the elderly, and those with underlying medical conditions such as chronic lung disease.[16,19] Influenza types A and B can cause human epidemics; however, in the case of most human pandemics, novel strain emergence and a greater overall disease burden is attributed to type A.[12,16] In the 2018-2019 season, less than 1% of influenza cases in Europe were attributed to type B, and a similar dominance of type A was also reported in the United States.

Respiratory syncytial virus (RSV) is another leading cause of lower respiratory tract infections and hospitalizations in infants and children,[17,20] with most children having an RSV infection by two years of age.[21] In children five years of age or younger, there are over three million hospitalizations and over 100,000 globally estimated deaths from lower respiratory RSV infections.[17] More recently, due in part to diagnostic improvements, RSV has also been associated with a substantial disease and health economic burden in older adults as well.[22-24]

Effective diagnosis and differentiation of influenza, RSV, and SARS-CoV-2 infection from one another and from other respiratory pathogens in vulnerable patients is needed to address the substantial burden of illness.[25] 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.[26] 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.[27-29]

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.[30,31] 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.[13,20,32] The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test uses real-time PCR instrument technology to rapidly (in approximately 20 minutes) detect viral RNA from both nasopharyngeal swabs and anterior nasal swabs.[33] The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test allows for the differential diagnosis of all 4 viral infections in symptomatic individuals suspected of infection by their healthcare provider.

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 Process Control (IPC) is also included. The IPC is present 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.
- For use under Emergency Use Authorization (EUA) only
- In the United States:
    - This product has not been FDA cleared or approved but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.
    - This product has been authorized only for the detection and differentiation of nucleic acid from SARS-CoV-2, influenza A, influenza B, and RSV, not for any other viruses or pathogens.
    - The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high, moderate, or waived complexity tests. This test is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.
- 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 **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.[34,35]
- If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected using appropriate infection control precautions for novel virulent influenza viruses and sent to state health departments for testing. Virus culture should not be attempted in these cases unless a 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 Roche representative.
- Use only the transfer pipettes contained in the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay pack. Use of alternative transfer pipettes may lead to invalid results.
- Carefully adhere to the procedures specified in this Testing Instructions document. Wear laboratory gloves, laboratory coat, and eye protection when handling samples and reagents. Change gloves before removing transfer pipette from the **cobas®** 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.
- Performance characteristics have been determined with specimens from human patients with signs and symptoms of respiratory infection.

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.

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 for colder) if testing within 72 hours is not possible.

  Note: Specimens collected in saline should not be frozen.
- Once samples have 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, with storage at room temperature (15-30 °C).
- 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. 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 in this media types was not established.

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 Process 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

Reagents in cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic test assay tube	**Reagent ingredients**	**Safety symbol and warning[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 9002-92-0 Polidocanol
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	N/A
cobas® liat SARS-CoV-2, Influenza A/B & RSV 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

Reagents in cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic test assay tube	Reagent ingredients	Safety symbol and warning[a]
cobas® liat SARS-CoV-2, Influenza A/B & RSV 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 SARS-CoV-2, Influenza A/B & RSV 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 primarily follows EU GHS guidance
[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 negative/positive control 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 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: Materials provided

P/N	Material description	Quantity	Storage temperature	Storage time
09731261190	**cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test (assay tubes)	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

*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 one week at room temperature. Kits should be labeled with the start date of room temperature storage and disposed of if not used within one week.

Materials required but not provided

Table 4: Materials required but not provided

Specimen Collection Kit	P/N
Nasopharyngeal Swab Collection Kits: Flexible minitip FLOQSwab™ with Universal Transport Media™ (UTM®) from Copan Diagnostics OR BD™ Universal Viral Transport (UVT) 3-mL collection kit with a flocked flexible minitip swab	305C, 307C, 321C, 3C057N, 3C071N 220529, 220531
Nasal Swab Collection Kits: Regular FLOQSwab™ with Universal Transport Media™ (UTM®) from Copan Diagnostics, OR BD™ Universal Viral Transport (UVT) 3-mL collection kit with a regular flocked swab, OR Copan Universal Transport Medium (UTM-RT®), without beads	306C, 321C, 346C, 3C064N 220527, 220528 3C047N, 3C075N
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 in 10 mL Tube, 50 Tubes per Pack	20A00K984

*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. 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 in this media types was not established.

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 version 3.4 or higher
cobas® liat SARS-CoV-2, Influenza A/B & RSV script (CFRA) v1.0.8 (EUA) 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 nucleic acid test 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 nucleic acid test assay tube. Do not use a **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 nucleic acid test assay tube during or after the run on the **cobas® liat** analyzer.
- Dispose of a used **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube, pipette and sample tube according to your institution's safety guidelines for hazardous material.

Procedural limitations

- The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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. 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. The clinical performance of the assay in these media types is unknown.
- Users in a point of care environment should not prepare (formulate, measure, aliquot) 0.9% physiological saline. CLIA certified moderate and high complexity laboratories may prepare and package equivalent 3 mL of physiological saline for use with **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test, but performance with these alternative solutions has not been established. When using physiological saline solution, ensure that the collection tube is an appropriate height for the swab such that the score mark on the swab is not higher than the height of the tube.
- As with other tests, negative results do not preclude SARS-CoV-2, Influenza A, Influenza B, or RSV 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® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- Recent administration of nasal vaccines (e.g., FluMist®) within 6 weeks prior to collection were not evaluated; **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test may detect the agents in those vaccines which may not represent infection by those viruses.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2, influenza A, influenza B, or RSV and their prevalence, which change over time.

Conditions of authorization for the laboratory

The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website:

- https://www.fda.gov/medical-devices/covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2

However, to assist clinical laboratories using the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test, the relevant Conditions of Authorization are listed below:

- Authorized laboratories* using the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test must include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using **cobas® liat** SARS-CoV-2, Influenza A/B & RSV must use the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test are not permitted.
- Authorized laboratories that receive the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test must notify the relevant public health authorities of their intent to run the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test prior to initiating testing.
- Authorized laboratories using the **cobas® liat** SARS-CoV-2-CoV-2, Influenza A/B & RSV nucleic acid test must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories must collect information on the performance of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test and must report any significant deviations from the established performance characteristics of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test of which they become aware to DMD/OHT7/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Roche (https://www.roche.com/about/business/roche_worldwide.htm; US customers can also report by phone at 1-800-800-5973).
- All operators using the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test must be appropriately trained in performing and interpreting the results of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test, use appropriate personal protective equipment when handling this kit, and must use the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test in accordance with the authorized labeling.
- Roche, authorized distributor(s) and authorized laboratories using the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records must be made available to FDA for inspection upon request.

*The letter of authorization refers to "authorized laboratories" as "laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high, moderate or waived complexity tests. The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation."

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

Before using a new lot of **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 nucleic acid test 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 nucleic acid test assay tubes from this lot □ 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

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 in **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test kit.
5	Choose **Scan** and scan the negative control barcode from the negative/positive control barcode card 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 nucleic acid test 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 of the transfer pipette and control tube as biohazardous material. ***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 SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube kit to transfer controls and samples into the cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test tubes.*** ***Note: Do not puncture the cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 nucleic acid test assay tube and the transfer pipette, and restart the testing procedure with a new cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube, negative control, and pipette.***
7	Choose **Scan**, and scan the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 discard the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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. In Step 6, transfer the control from the positive control tube.*** 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 nucleic acid test sample testing workflow

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

- □ 1 **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 nucleic acid test assay tube, and one of the transfer pipettes provided. ***Note: Only use the transfer pipette provided in the cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube packs to transfer samples into the cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube.***
4	From the **Main** menu, choose **Run Assay** and choose the **Select** button. Then **Scan** the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 nucleic acid test assay tube. Using a transfer pipette provided in the packs, 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 of the transfer pipette as biohazardous material. ***Note: Do not puncture the cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 nucleic acid test assay tube and the transfer pipette, and restart the testing procedure with a new cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube and pipette.***
7	Choose **Scan**, and rescan the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test 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 nucleic acid test assay tube when stored at room temperature (step 6).***
8	When the assay test run is complete, remove and discard the used **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tube as biohazardous material.
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.

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® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tubes that has already been added through the "Lot Validation" workflow. Use the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV Control Kit to conduct these runs.

Materials needed for additional control runs

- **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test assay tubes
- 1 transfer pipette per control run
- **cobas® liat** SARS-CoV-2, Influenza A/B & RSV positive controls and/or negative controls
- Corresponding barcodes for the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV positive controls and/or the negative controls

Additional control runs workflow

Follow the procedures outlined under the section "**cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test sample testing workflow" to perform additional control runs. In step 3, be sure to use the provided control barcodes 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 nucleic acid test 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 nucleic acid test 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 nucleic acid test 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 (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 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. Each strain evaluated as well as the corresponding LoD 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)

A 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, 20 influenza A (10 H1N1 & 10 H3N2), ten (10) influenza B (5 Victoria and 5 Yamagata), and six (6) RSV isolates/variants. All strains were individually tested at 3x LoD in 3 replicates to demonstrate 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 tested in the study and the lowest concentrations detected are listed in Table 9.

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

Lineage/Subtype*	Isolate/Variant	Test Concentration ($TCID_{50}$/mL)
Alpha	Hong Kong/VM20001061/2020	0.105
Beta, B.1.595_2020 (was B.1.2)	NY-Wadsworth-33126-01/2020	0.105
Delta, B.1.617.2	USA/MD-HP05285/2021	0.105
Epsilon, B.1.427	USA/CA/VRLC009/2021	0.105
Gamma, P.1	Japan/TY7-503/2021	0.105
Iota, B.1.526_2021	USA/NY-Wadsworth-21025952-01/2021	0.105
Kappa, B.1.617.1	USA/CA-Stanford-15_S02/2021	0.105
Omicron, B.1.1.529, CH.1.1	USA/MD-HP41275/2022	0.105
Omicron, B.1.1.529, XBB.1.5	USA/MD-HP40900/2022	0.105
Zeta, P2_2021	USA/NY-Wadsworth-21006055-01/2021	0.105

*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.

In addition, *in silico* analysis (as of September 2023) of SARS-CoV-2 sequences indicates that >99.9% of sequences for SARS-CoV-2 have ≤ 2 mismatches/changes in primer/probe binding sites at both target regions simultaneously. *In silico* analysis of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test included analysis of CDC-recommended vaccine strains and sequence alignments of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test primers and probes with the SARS-CoV-2 vaccine strains show that all 2023-2024 vaccine strains are predicted to be detected.

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)
H1N1	A/Brisbane/59/07	0.885
H1N1	A/Christ Church/16/2020	1.77
H1N1	A/Denver/01/57	0.885
H1N1	A/Fort Monmouth/01/47	0.885
H1N1	A/Malaya/302/54	0.885
H1N1	A/New Caledonia/20/99	0.885

Lineage/Subtype*	Isolate/Variant**	Test Concentration ($TCID_{50}$/mL)
H1N1	A/Swine/Iowa/15/30	1.77
H1N1	A/Sydney/5/2021	1.77
H1N1	A/Victoria/2570/2019	3.54
H1N1	A/WS/33	0.885
H1N1	A/Brisbane/14/2023	75‡
H1N1	A/Townsville/1A/2023	75‡
H1N1	A/ Townsville/2A/2023	75‡
H3N2	A/Aichi/2/68	0.885
H3N2	A/Brisbane/10/07	0.885
H3N2	A/Cambodia/E0826360/2020	0.885
H3N2	A/Darwin/9/2021	1.77
H3N2	A/Hong Kong/8/68	0.885
H3N2	A/H3/Perth/16/09	0.885
H3N2	A/Tasmania/503/2020	0.885
H3N2	A/Victoria/3/75	0.885
H3N2	A/Wisconsin/67/2005	0.885
H3N2	A/Singapore/INFIMH-16-0019/2016	0.885

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

Three influenza A strains: A/England/33/2022, A/England/55/2022 and A/England/73/2022 were also tested and detected by the **cobas® liat SARS-CoV-2, Influenza A/B & RSV nucleic acid test.

‡copies/mL

In addition, *in silico* analysis (as of September 2023) of influenza A sequences indicates that >99.9% of sequences for influenza A have ≤ 2 mismatches/changes in primer/probe binding sites at the target region. Sequence alignments of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test primers and probe with the WHO-recommended influenza A H1N1 and H3N2 vaccine strains for 2023-2024 were included in the *in silico* analysis and are predicted to be detected.

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)
Victoria	B/Brisbane/60/2008	2.937
Victoria	B/Colorado/06/2017	2.937
Victoria	B/Malaysia/2506/04	2.937
Victoria	B/Michigan/09/2011	2.937
Victoria	B/Washington/02/2019	2.937
Yamagata	B/Florida/04/06	2.937
Yamagata	B/Massachusetts/2/2012	2.937
Yamagata	B/Texas/6/2011	2.937
Yamagata	B/Texas/81/2016	2.937
Yamagata	B/Wisconsin/1/2010	2.937

*These strains are in addition to the influenza B Austria/1359417/2021 and Phuket/3073/2013 strains used in the analytical sensitivity study.

In addition, *in silico* analysis (as of September 2023) of influenza B sequences indicates that >99.9% of sequences for influenza B have ≤ 2 mismatches/changes in primer/probe binding sites at the target region. Sequence alignments of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV assay primers and probe with the WHO-recommended influenza B vaccine strains for 2023-2024 were included in the *in silico* analysis and are predicted to be detected.

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)
RSV-A	RSV-A 2006 isolate	0.807
RSV-A	RSV-A2	0.807
RSV-B	RSV-B Ch93(18)-18	0.807
RSV-B	RSV-B Wash/18537/62	0.807
RSV-B	RSV-B WV/14617/85	0.807

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

In addition, *in silico* analysis (as of September 2023) of RSV sequences indicates that >99.9% of sequences for RSV have ≤ 2 mismatches/changes in primer/probe binding sites at the target region.

Cross reactivity and microbial interference

Cross-reactivity and microbial interference of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test were evaluated by testing a panel of microorganisms. High titer stocks of the potentially cross-reacting microorganisms were tested for cross-reactivity with **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test, and also in the presence of SARS-CoV-2, influenza A, influenza B, and RSV at 3x LoD concentrations and tested for microbial interference. Three (3) replicates in target positive background and three (3) replicates in target negative background were tested for each non-target microorganism. The testing concentrations for potentially interfering microorganisms are ≥1.0E+05 units/mL for viruses and ≥1.0E+06 units/mL for other microorganisms unless otherwise noted (Table 13).

None of the organisms tested interfered or cross reacted with **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test performance at the concentrations tested.

Table 13: List of microorganisms tested for cross-reactivity and microbial interference with the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test

Type	Microorganism	Test Concentration†	Unit
Virus	Adenovirus Type 1	1.00E+05	$TCID_{50}$/mL
Virus	Cytomegalovirus	1.00E+05	cp/mL
Virus	Epstein-Barr virus	1.00E+05	cp/mL
Virus	Human Coronavirus OC43	1.00E+05	$TCID_{50}$/mL
Virus	Human Coronavirus 229E	1.00E+05	$TCID_{50}$/mL
Virus	Human Rhinovirus Type 1A	7.05E+04*	$TCID_{50}$/mL
Virus	Measles	1.00E+05	$TCID_{50}$/mL
Virus	Human Enterovirus 68	1.00E+05	$TCID_{50}$/mL
Virus	Human Parainfluenza Virus Type 2	1.00E+05	$TCID_{50}$/mL
Virus	Human Parainfluenza Virus Type 3	1.00E+05	$TCID_{50}$/mL
Virus	SARS Coronavirus, Urbani	2.85E+04*	Genome equivalents/mL
Virus	Human Coronavirus NL63	1.00E+05	$TCID_{50}$/mL
Virus	MERS-Coronavirus	1.00E+05	$TCID_{50}$/mL
Virus	Adenovirus Type 7	1.00E+05	$TCID_{50}$/mL
Virus	Human Parainfluenza Virus Type 4A	5.85E+04*	$TCID_{50}$/mL
Virus	Human Parainfluenza Virus Type 1	1.00E+05	$TCID_{50}$/mL
Virus	Human Metapneumovirus 27	1.00E+05	$TCID_{50}$/mL
Virus	Mumps	1.00E+05	$TCID_{50}$/mL
Virus	Human Rhinovirus B	1.00E+05	$TCID_{50}$/mL
Bacteria	*Bordetella pertussis*	1.00E+06	CFU/mL
Bacteria	*Corynebacterium flavescens*	1.00E+06	CFU/mL
Bacteria	*Escherichia coli*	1.00E+06	CFU/mL
Bacteria	*Haemophilus influenzae*	1.00E+06	CFU/mL
Bacteria	*Lactobacillus crispatus*	1.00E+06	CFU/mL
Bacteria	*Legionella pneumophila*	1.00E+06	CFU/mL
Bacteria	*Moraxella catarrhalis*	1.00E+06	CFU/mL

Type	Microorganism	Test Concentration†	Unit
Bacteria	*Mycoplasma pneumonia*e	1.00E+06	CFU/mL
Bacteria	*Neisseria elongata*	1.00E+06	CFU/mL
Bacteria	*Neisseria meningitidis*	1.00E+06	CFU/mL
Bacteria	*Pseudomonas aeruginosa*	1.00E+06	CFU/mL
Bacteria	*Staphylococcus aureus*	1.00E+06	CFU/mL
Bacteria	*Staphylococcus epidermidis*	1.00E+06	CFU/mL
Bacteria	*Streptococcus pneumoniae*	1.00E+06	CFU/mL
Bacteria	*Streptococcus pyogenes*	1.00E+06	CFU/mL
Bacteria	*Streptococcus salivarius*	1.00E+06	CFU/mL
Bacteria	*Chlamydophila pneumoniae*	1.00E+06	IFU/mL
Bacteria	*Fusobacterium necrophorum* subsp. *necrophorum*	1.00E+06	CFU/mL
Bacteria	*Neisseria flava*	1.00E+06	CFU/mL
Bacteria	*Bordetella parapertussis*	1.00E+06	CFU/mL
Bacteria	*Mycobacterium tuberculosis*	1.00E+06	CFU/mL
Bacteria	*Mycoplasma genitalium*	1.00E+06	cp/mL
Fungus	*Candida albicans*	1.00E+06	CFU/mL
Fungus	*Aspergillus flavus* var. *flavus*	1.00E+06	CFU/mL

* Tested at highest concentration available

† Clinical specimens containing Human Coronavirus HKU1 and *Pneumocystis jirovecii* were also tested and did not cross-react or interfere with the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test; test concentration was unknown.

Competitive inhibition (co-infection)

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

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.

Table 15: Endogenous and Exogenous Interference

Potential Interferent	Active Ingredient	Concentration Tested
Peripheral blood mononuclear cell (PBMC)	-	1.00E+06 cell/mL
Mucin	Purified mucin protein	5 mg/mL
Human Whole Blood	-	5% v/v
Nasal spray - Afrin / Anefrin	Oxymetazoline	15% 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 ointment	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
Intranasal Vaccine – FluMist*	Live Quadrivalent 2022-2023 A/Victoria/1/2020 (H1N1) (an A/Victoria/2570/2019 (H1N1) pdm09 - like virus), A/Norway/16606/2021 (H3N2) (an A/Darwin/9/2021 (H3N2) - like virus), B/Phuket/3073/2013 (B/Yamagata lineage), and B/Austria/1359417/2021 (B/Victoria lineage) lineage)	6.25% (v/v)

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

Media equivalency – UTM, Remel Media, and Saline

Media equivalency was evaluated by spiking cultured viruses (SARS-CoV-2, influenza A, influenza B, and RSV) at ~1-2x and ~5x LoD into natural clinical NPS collected in UTM, M4RT and Saline (0.9% NaCl) in addition to negative samples. Pooled negative clinical specimens and contrived positive clinical specimens were tested with the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test. For each matrix, 10 replicates of negative samples, 30 replicates of positive samples at ~1-2x LoD and 10 replicates of positive samples at ~5x LoD were tested. The results showed that the assay was able to correctly detect the presence of the viral targets suspended in all media types (Table 16) demonstrating that UTM, M4RT media, and saline are acceptable collection and transport media for use with the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test.

Table 16: Summary of media equivalency study results

Collection Media	Concentration	SARS-CoV-2	Influenza A	Influenza B	RSV
UTM	Negative	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
UTM	~1-2x	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
UTM	~5x	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)
M4RT	Negative	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
M4RT	~1-2x	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
M4RT	~5x	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)
0.9% Saline	Negative	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
0.9% Saline	~1-2x	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
0.9% Saline	~5x	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)

Performance around LoD (reproducibility)

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 two (2) study sites representative of CLIA-waived intended use settings. Two (2) operators at each of the two sites tested a 3-member reproducibility panel in triplicate on five different days for three 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 panel member is "Detected." Percent agreement with expected result is shown in Table 17.

Table 17: 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 n	Percent Agreement n/N x 100	95% Score CI
Negative	0	175	175	100.0	(97.9, 100.0)
SARS-CoV-2	1x-2x LoD	180	180	100.0	(97.9, 100.0)
SARS-CoV-2	3x-5x LoD	177	177	100.0	(97.9, 100.0)
Influenza A	1x-2x LoD	180	180	100.0	(97.9, 100.0)
Influenza A	3x-5x LoD	177	177	100.0	(97.9, 100.0)
Influenza B	1x-2x LoD	180	179	99.4	(96.9, 99.9)
Influenza B	3x-5x LoD	177	177	100.0	(97.9, 100.0)
RSV	1x-2x LoD	180	180	100.0	(97.9, 100.0)
RSV	3x-5x LoD	177	177	100.0	(97.9, 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.

Clinical performance evaluation

The clinical performance of the **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test was evaluated using archived clinical nasopharyngeal swab (NPS) and nasal swab (NS) specimens in Universal Viral Transport medium (UVT) or Universal Transport Medium (UTM). 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 nucleic acid test to the results of a comparator method that utilized FDA-cleared Nucleic Acid Amplification Test (NAAT) for the SARS-CoV-2, influenza A, influenza B, and RSV targets.

Of 211 NPS samples tested on the comparator method, all were evaluable for the clinical performance analysis for the SARS-CoV-2 target and one (1) was non-evaluable for influenza A, influenza B, and RSV targets due to invalid result for these targets on **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test. Additionally, two (2) NPS samples were non-evaluable for influenza A due to obtaining inconclusive results on the comparator method for this analyte. The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test demonstrated a PPA and NPA of 96.7% and 96.7% for SARS-CoV-2, respectively; 100% and 98.1% for influenza A, respectively; 100% and 97.7% for influenza B, respectively; and 100% and 97.2% for RSV, respectively.

Of 206 NS samples tested on the comparator method, all were evaluable for the clinical performance analysis for the SARS-CoV-2, influenza B and RSV targets and 205 were evaluable for the influenza A target due to one (1) inconclusive result on the comparator method for this analyte. The **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test demonstrated a PPA and NPA of 100% and 98.9% for SARS-CoV-2, respectively; 100% and 98.0% for influenza A, respectively; 100% and 98.3% for influenza B, respectively; and 100% and 97.7% for RSV, respectively.

Table 18: Clinical Performance for **cobas® liat** SARS-CoV-2, Influenza A/B & RSV nucleic acid test by Target and Specimen Type

Target	Specimen Type	Total	TP /(TP+FN)	PPA (95% CI)	TN/(TN+FP)	NPA (95% CI)
SARS-CoV-2	NPS	211	29/30	**96.7%** (83.3%, 99.4%)	175/181	**96.7%** (93.0%, 98.5%)
SARS-CoV-2	NS	206	30/30	**100%** (88.6%, 100%)	174/176	**98.9%** (96.0%, 99.7%)
Influenza A	NPS	208	53/53	**100%** (93.2%, 100%)	152/155	**98.1%** (94.5%, 99.3%)
Influenza A	NS	205	52/52	**100%** (93.1%, 100%)	150/153	**98.0%** (94.4%, 99.3%)
Influenza B	NPS	210	34/34	**100%** (89.8%, 100%)	172/176	**97.7%** (94.3%, 99.1%)
Influenza B	NS	206	34/34	**100%** (89.8%, 100%)	169/172	**98.3%** (95.0%, 99.4%)
RSV	NPS	210	32/32	**100%** (89.3%, 100%)	173/178	**97.2%** (93.6%, 98.8%)
RSV	NS	206	34/34	**100%** (89.8%, 100%)	168/172	**97.7%** (94.2%, 99.1%)

Note: TP = True Positive; FN = False Negative; TN = True Negative; FP = False Positive; CI = Confidence Interval; NPS = Nasopharyngeal swab; NS = Nasal swab

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 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

Additional information

Key test features

Sample type	Nasopharyngeal and Nasal swab samples collected in the Copan UTM-RT System, the BD™ UVT System, the Thermo Fisher™ Scientific Remel™ System, or in 0.9% 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

Table 20: Symbols are used in labeling for Roche PCR assays

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 US Only: Federal law restricts this device to sale by or on the order of a physician.
CONTROL Control	Patient number	Use-by date
Date of manufacture	Peel here	
Device for near-patient testing	CONTROL + Positive control	
Device for self-testing	QS copies / PCR QS copies per PCR reaction, use the QS copies per PCR reaction in calculation of the results.	

Technical support

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

Manufacturer and distributor

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1080 US Highway 202 South
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