Rx Only

# cobas® SARS-CoV-2 & Influenza A/B v2

## Qualitative assay for use on the cobas ® 6800/8800 Systems

*For use under Emergency Use Authorization (EUA) only*

*For in vitro diagnostic use*

| | |
|---|---|
| cobas® SARS-CoV-2 & Influenza A/B v2 | P/N: 10033401190 |
| cobas® SARS-CoV-2 & Influenza A/B Control Kit | P/N: 09446133190 |
| cobas® Buffer Negative Control Kit | P/N: 09051953190 |

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# Summary and explanation of the test

## Intended use

cobas® SARS-CoV-2 & Influenza A/B v2 assay for use on the cobas® 8800/8800 Systems (cobas® SARS-CoV-2 & Influenza A/B v2) is an automated multiplex real-time RT-PCR assay intended for simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A virus, and influenza B virus RNA in healthcare provider-collected nasal and nasopharyngeal swab specimens, and self-collected anterior nasal swab specimens (collected in a healthcare setting with instruction by a healthcare provider) from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. cobas® SARS-CoV-2 & Influenza A/B v2 is intended for use as an aid in the differential diagnosis of SARS-CoV-2, influenza A, and influenza B in humans and is not intended to detect influenza C. 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 moderate or high complexity tests.

RNA from SARS-CoV-2, influenza A, and influenza B is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2, influenza A, and/or influenza B 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 viruses. The agent detected may not be the definite cause of disease. Testing facilities within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.

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

cobas® SARS-CoV-2 & Influenza A/B v2 is intended for use by qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time RT-PCR and on the use of the cobas® 8800/8800 Systems. In the United States, cobas® SARS-CoV-2 & Influenza A/B v2 is only for use under the Food and Drug Administration's Emergency Use Authorization.

## Explanation of the test

cobas® SARS-CoV-2 & Influenza A/B v2 is a qualitative test for the use on the cobas® 8800 System and cobas® 8800 System for the detection of the 2019 novel coronavirus (SARS-CoV-2), influenza A, and influenza B RNA in both anterior nasal and nasopharyngeal swab samples collected in Copan Universal Transport Medium System (UTM-RT®) or BD™ Universal Viral Transport System (UVT) and additionally for nasal swab samples collected in cobas® PCR Media or 0.9% physiological saline. The RNA Internal Control, used to monitor the entire sample preparation and PCR amplification process, is introduced into each specimen during sample processing. In addition, the test utilizes external controls (a low titer positive control and a negative control).

## Principles of the procedure

cobas® SARS-CoV-2 & Influenza A/B v2 is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. The cobas® 6800/8800 Systems consist of the sample supply module, the transfer module, the processing module, and the analytic module. Automated data management is performed by the cobas® 6800/8800 software, which assigns results for all tests. Results can be reviewed directly on the system screen, and printed as a report.

Nucleic acid from patient samples and added internal control RNA (RNA IC) molecules are simultaneously extracted. Nucleic acid is released by addition of proteinase and lysis reagent to the sample. The released nucleic acid binds to the silica surface of the added magnetic glass particles. Unbound substances and impurities, such as denatured protein, cellular debris and potential PCR inhibitors are removed with subsequent wash steps and purified nucleic acid is eluted from the magnetic glass particles with elution buffer at elevated temperature. External controls (positive and negative) are processed in the same way with the cobas® SARS-CoV-2 & Influenza A/B v2 run.

Selective amplification of SARS-CoV-2 target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for ORF1a/b non-structural region that is unique to SARS-CoV-2. Additionally, a conserved region in the structural protein envelope E-gene was chosen for pan-Sarbecovirus detection. The pan-Sarbecovirus detection set will also detect SARS-CoV-2 virus. For influenza A, selective amplification of target nucleic acid from the sample is achieved by the use of two target-specific sets of forward and reverse primers, one for the genomic region encoding matrix proteins 1 and 2 (M1/M2) and one for the gene encoding polymerase basic protein 2 (PB2). For influenza B, selective amplification of target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for the nuclear export protein (NEP) / nonstructural protein 1 (NS1) genomic region. Selective amplification of RNA Internal Control is achieved by the use of non-competitive sequence specific forward and reverse primers which have no homology with the coronavirus or influenza genomes. Amplified target is detected by cleavage of fluorescently labeled oligonucleotide probes. A thermostable DNA polymerase enzyme is used for amplification.

The cobas® SARS-CoV-2 & Influenza A/B v2 master mix contains detection probes which are specific for the coronavirus type SARS-CoV-2, members of the Sarbecovirus subgenus, influenza A virus, influenza B virus and the RNA Internal Control nucleic acid. The coronavirus, influenza A, influenza B and RNA Internal Control detection probes are each labeled with unique fluorescent dyes that act as a reporter. Each probe also has a second dye which acts as a quencher. When not bound to the target sequence, the fluorescent signals of the intact probes are suppressed by the quencher dye. During the PCR amplification step, hybridization of the probes to the specific single-stranded DNA template results in cleavage of the probe by the 5' to 3' exonuclease activity of the DNA polymerase resulting in separation of the reporter and quencher dyes and the generation of a fluorescent signal. With each PCR cycle, increasing amounts of cleaved probes are generated and the cumulative signal of the reporter dye increases concomitantly. Each reporter dye is measured at defined wavelengths, which enables simultaneous detection and discrimination of the amplified coronavirus targets, influenza targets and the RNA Internal Control. The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythimidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon). Any contaminating amplicons from previous PCR runs are destroyed by the AmpErase enzyme [uracil-N-glycosylase], which is included in the PCR mix, when heated in the first thermal cycling step. However, newly formed amplicons are not destroyed since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

# Reagents and materials

The materials provided for cobas® SARS-CoV-2 & Influenza A/B v2 can be found in Table 1. Materials required, but not provided can be found in Table 2, Table 3, Table 4, Table 7, Table 8 and Table 9.

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

## cobas® SARS-CoV-2 & Influenza A/B v2 reagents and controls

All unopened reagents and controls shall be stored as recommended in Table 1 to Table 4.

**Table 1 cobas® SARS-CoV-2 & Influenza A/B v2**

**(SCoV2-FluA/B v2)**

Store at 2-8°C
192 test cassette (P/N 10033401190)

| Kit components | Reagent ingredients | Quantity per kit 192 tests |
|---|---|---|
| **Proteinase Solution (PASE)** | Tris buffer, < 0.05% EDTA, calcium chloride, calcium acetate, 8% proteinase, glycerol<br>EUH210: Safety data sheet available on request.<br>EUH208: Contains Subtilisin from *Bacillus subtilis*. May produce an allergic reaction. | 22.3 mL |
| **RNA Internal Control (RNA IC)** | Tris buffer, <0.05% EDTA, <0.001% non-target related armored RNA construct containing primer and probe specific sequence regions (non-infectious RNA in MS2 bacteriophage), <0.1% sodium azide | 21.2 mL |
| **Elution Buffer (EB)** | Tris buffer, 0.2% methyl-4 hydroxybenzoate | 21.2 mL |
| **Master Mix Reagent 1 (MMX-R1)** | Manganese acetate, potassium hydroxide, < 0.1% sodium azide | 7.5 mL |
| **SCoV2-FluA/B v2 Master Mix Reagent 2 (SCoV2-FluA/B v2 MMX-R2)** | Tricine buffer, potassium acetate, < 18% dimethyl sulfoxide, glycerol, < 0.1% Tween 20, EDTA, < 0.15% dATP, dCTP, dGTP, dUTPs, < 0.01% upstream and downstream SARS-CoV-2, Sarbecovirus, influenza A and influenza B primers, < 0.01% Internal Control forward and reverse primers, < 0.01% fluorescent-labeled oligonucleotide probes specific for SARS-CoV-2, Sarbecovirus, influenza A, influenza B and the RNA Internal Control, < 0.01% oligonucleotide aptamer, < 0.1% Z05D DNA polymerase, < 0.10% AmpErase (uracil-N-glycosylase) enzyme (microbial), < 0.1% sodium azide | 9.7 mL |

**Table 2** cobas® SARS-CoV-2 & Influenza A/B Control Kit

**(SCoV2-FluA/B CTL)**

Store at 2–8°C

(P/N 09446133190)

| Kit components | Reagent ingredients | Quantity per kit |
|---|---|---|
| **SCoV2-FluA/B Positive Control (SCoV2-FluA/B (+) C)** | Tris buffer, < 0.05% Sodium azide, < 0.005% EDTA, < 0.003% Poly rA, < 0.01% Non-infectious plasmid DNA (microbial) containing SARS-CoV-2 sequence, < 0.01% Non-infectious plasmid DNA (microbial) containing pan-Sarbecovirus sequence, < 0.01% Non-infectious plasmid DNA (microbial) containing influenza A sequence, < 0.01% Non-infectious plasmid DNA (microbial) containing influenza B sequence | 16 mL (16 x 1 mL) |

**Table 3** cobas® Buffer Negative Control Kit

**(BUF (-) C)**

Store at 2-8°C

(P/N 09051953190)

| Kit components | Reagent ingredients | Quantity per kit |
|---|---|---|
| **cobas® Buffer Negative Control (BUF (-) C)** | Tris buffer, < 0.1% sodium azide, EDTA, < 0.002% Poly rA RNA (synthetic) | 16 mL (16 x 1 mL) |

# cobas® omni reagents for sample preparation

**Table 4 cobas® omni** reagents for sample preparation*

| Reagents | Reagent ingredients | Quantity per kit | Safety symbol and warning** |
|---|---|---|---|
| **cobas® omni MGP Reagent (MGP)**<br>Store at 2–8°C<br>(P/N 06997546190) | Magnetic glass particles, Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide | 480 tests | Not applicable |
| **cobas® omni Specimen Diluent (SPEC DIL)**<br>Store at 2–8°C<br>(P/N 06997511190) | Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide | 4 x 875 mL | Not applicable |
| **cobas® omni Lysis Reagent (LYS)**<br>Store at 2–8°C<br>(P/N 06997538190) | 43% (w/w) guanidine thiocyanate***, 5% (w/v) polydocanol***, 2% (w/v) dithiothreitol***, dihydro sodium citrate | 4 x 875 mL |  <br>**DANGER**<br>H302: Harmful if swallowed.<br>H314: Causes severe skin burns and eye damage.<br>H412: Harmful to aquatic life with lasting effects.<br>EUH032: Contact with acids liberates very toxic gas.<br>EUH071: Corrosive to the respiratory tract.<br>P273: Avoid release to the environment.<br>P280: Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection.<br>P301 + P330 + P331: IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.<br>P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.<br>P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor.<br>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.<br>593-84-0 Guanidinium thiocyanate<br>9002-92-0 Polidocanol<br>3483-12-3 (R*,R*)-1,4-dimercaptobutane-2,3-diol |
| **cobas® omni Wash Reagent (WASH)**<br>Store at 15–30°C<br>(P/N 06997503190) | Sodium citrate dihydrate, 0.1% methyl-4 hydroxybenzoate | 4.2 L | Not applicable |

* These reagents are not included in cobas® SARS-CoV-2 & Influenza A/B 2 test kits. See listing of additional materials required (Table 7, Table 8 and Table 9).

** Product safety labeling primarily follows EU GHS guidance

***Hazardous substance

## Reagent storage and handling requirements

Reagents shall be stored and will be handled as specified in Table 5 and Table 6.

When reagents are not loaded on the cobas® 6800/8800 System, store them at the corresponding temperature specified in Table 5.

**Table 5** Reagent storage (when reagent is not on the system)

| Reagent | Storage temperature |
|---|---|
| cobas® SARS-CoV-2 & Influenza A/B v2 | 2–8°C |
| cobas® SARS-CoV-2 & Influenza A/B Control Kit | 2–8°C |
| cobas® Buffer Negative Control Kit | 2–8°C |
| cobas® omni Lysis Reagent | 2–8°C |
| cobas® omni MGP Reagent | 2–8°C |
| cobas® omni Specimen Diluent | 2–8°C |
| cobas® omni Wash Reagent | 15–30°C |

Reagents loaded onto the cobas® 6800/8800 Systems are stored at appropriate temperatures and their expiration is monitored by the system. The cobas® 6800/8800 Systems allow reagents to be used only if all of the conditions shown in Table 6 are met. The system automatically prevents use of expired reagents. Table 6 allows the user to understand the reagent handling conditions enforced by the cobas® 6800/8800 Systems.

**Table 6** Reagent expiry conditions enforced by the cobas® 6800/8800 Systems

| Reagent | Kit expiration date | Open-kit stability | Number of runs for which this kit can be used | On-board stability (cumulative time on board outside refrigerator) |
|---|---|---|---|---|
| cobas® SARS-CoV-2 & Influenza A/B v2 | Date not passed | 90 days from first usage[a] | Max 40 runs[a] | Max 40 hours[a] |
| cobas® SARS-CoV-2 & Influenza A/B Control Kit | Date not passed | Not applicable[b] | Not applicable | Max 8 hours |
| cobas® Buffer Negative Control Kit | Date not passed | Not applicable[b] | Not applicable | Max 10 hours |
| cobas® omni Lysis Reagent | Date not passed | 30 days from loading[c] | Not applicable | Not applicable |
| cobas® omni MGP Reagent | Date not passed | 30 days from loading[c] | Not applicable | Not applicable |
| cobas® omni Specimen Diluent | Date not passed | 30 days from loading[c] | Not applicable | Not applicable |
| cobas® omni Wash Reagent | Date not passed | 30 days from loading[c] | Not applicable | Not applicable |

[a] The performance has not been established for suggested use cycles and time, but is based on similar reagents used on the same system.

[b] Single use reagents

[c] Time is measured from the first time that reagent is loaded onto the cobas® 6800/8800 Systems.

## Additional materials required

**Table 7** Materials and consumables for use on cobas® 6800/8800 Systems

| Material | P/N |
|---|---|
| cobas® omni Processing Plate | 05534917001 |
| cobas® omni Amplification Plate | 05534941001 |
| cobas® omni Pipette Tips | 05534925001 |
| cobas® omni Liquid Waste Container | 07094388001 |
| cobas® omni Lysis Reagent | 06997538190 |
| cobas® omni MGP Reagent | 06997546190 |
| cobas® omni Specimen Diluent | 06997511190 |
| cobas® omni Wash Reagent | 06997503190 |
| Solid Waste Bag and Solid Waste Container<br>or<br>Solid Waste Bag With Insert and Kit Drawer | 07435967001 and 07094361001<br>or<br>08030073001 and 08387281001 |
| cobas® omni Secondary Tubes 13x75 (optional) | 06438776001 |
| cobas® PCR Media Tube Replacement Cap Kit | 07958056190 |
| cobas® PCR Media Disposable Tube Stand (optional) | 07958064190 |
| MPA RACK 13 or 16 MM[a] | N/A |
| RD5 RACK – RD Standard rack[a] | N/A |

[a] Please contact your local Roche representative for a detailed order list for sample racks, racks for clot detection and tips accepted on the instruments and compatible with the assay.

## Alternative collection kits for swab specimens for use on the cobas® 6800/8800 Systems

**Table 8** Alternative specimen collection kits used with cobas® SARS-CoV-2 & Influenza A/B v2

| Collection Kit | P/N |
|---|---|
| cobas® PCR Media Uni Swab Sample Kit | 07958030190 |
| cobas® PCR Media Dual Swab Sample Kit | 07958021190 |
| cobas® PCR Media 100 tube kit | 06466281190 |
| cobas® Uni Swab 100 Kit | 09205098190 |

## Instrumentation and software required

The cobas® 6800/8800 software and cobas® SARS-CoV-2 & Influenza A/B v2 analysis package (SW cobas® CoV2FluA/B ASAP) must be installed on the instrument(s). The Instrument Gateway (IG) server will be provided with the system.

**Table 9** Instrumentation

| Equipment | P/N |
|---|---|
| cobas® 6800 System (Moveable Platform) | 05524245001 and 06379672001 |
| cobas® 6800 System (Fixed Platform) | 05524245001 and 06379664001 |
| cobas® 8800 System | 05412722001 |
| Sample Supply Module | 06301037001 |
| Instrument Gateway | 06349595001 |

For additional information, please refer to the cobas® 6800/8800 Systems – User Assistance and/or User Guide.

# Precautions and handling requirements

## Warnings and precautions

As with any test procedure, good laboratory practice is essential to the proper performance of this assay. Due to the high sensitivity of this test, care should be taken to keep reagents and amplification mixtures free of contamination.

- For in vitro diagnostic use under the Food and Drug Administration's Emergency Use Authorization (EUA) only.
- For prescription use only.
- cobas® SARS-CoV-2 & Influenza A/B v2 has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 US.C. §263a, that meet requirements to perform moderate or high complexity tests.
- cobas® SARS-CoV-2 & Influenza A/B v2 has been authorized only for the detection and differentiation of nucleic acid from SARS-CoV-2, influenza A, and influenza B, not for any other viruses or pathogens.
- The emergency use of cobas® SARS-CoV-2 & Influenza A/B v2 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.
- Results (positive and negative) for influenza should be interpreted with caution. If an influenza result is inconsistent with clinical presentation and/or other clinical and epidemiological information, FDA-cleared Influenza NAATs are available for confirmation if clinically indicated
- Laboratories within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.
- All patient samples should be handled as if infectious, using good laboratory procedures as outlined in Biosafety in Microbiological and Biomedical Laboratories and in the CLSI Document M29-A4[12]. Only personnel proficient in handling infectious materials and the use of cobas® SARS-CoV-2 & Influenza A/B v2 and cobas® 6800/8800 Systems should perform this procedure.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions. If spillage occurs, immediately disinfect with a freshly prepared solution of 0.5% sodium hypochlorite (distilled or deionized water (dilute household bleach 1:10)) and follow appropriate site procedures.
- The use of sterile disposable pipettes and nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance
- Safety Data Sheets (SDS) are available on request from your local Roche representative.
- Closely follow procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect optimal test performance.
- False positive results may occur if carryover of samples is not adequately controlled during sample handling and processing.

## Reagent handling

- Handle all reagents, controls, and samples according to good laboratory practice in order to prevent carryover of samples or controls.
- Before use, visually inspect each reagent cassette, diluent, lysis reagent, and wash reagent to ensure that there are no signs of leakage. If there is any evidence of leakage, do not use that material for testing.
- cobas® omni Lysis Reagent contains guanidine thiocyanate, a potentially hazardous chemical. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur.
- cobas® SARS-CoV-2 & Influenza A/B v2 test kit, cobas® SARS-CoV-2 & Influenza A/B Control kit, cobas® Buffer Negative Control kit, cobas® omni MGP Reagent, and cobas® omni Specimen Diluent contain sodium azide as a preservative. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur. If these reagents are spilled, dilute with water before wiping dry.
- Do not allow cobas® omni Lysis Reagent, which contains guanidine thiocyanate, to contact sodium hypochlorite (bleach) solution. This mixture can produce a highly toxic gas.
- Dispose of all materials that have come in contact with samples and reagents in accordance with country, state, and local regulations.

## Good laboratory practice

- Do not pipette by mouth.
- Do not eat, drink, or smoke in designated work areas.
- Wear laboratory gloves, laboratory coats, and eye protection when handling samples and reagents. Gloves must be changed between handling samples and cobas® SARS-CoV-2 & Influenza A/B v2 kits, cobas® SARS-CoV-2 & Influenza A/B Control kit, cobas® Buffer Negative Control kit and cobas® omni reagents to prevent contamination. Avoid contaminating gloves when handling samples and controls.
- Wash hands thoroughly after handling samples and kit reagents, and after removing the gloves.
- Thoroughly clean and disinfect all laboratory work surfaces with a freshly prepared solution of 0.6% sodium hypochlorite in distilled or deionized water (dilute household bleach 1:10). Follow by wiping the surface with 70% ethanol.
- If spills occur on the cobas® 6800/8800 instrument, follow the instructions in the cobas® 6800/8800 Systems – User Assistance and/or User Guide to properly clean and decontaminate the surface of instrument(s).

# Sample collection, transport, and storage

**Note: Handle all samples and controls as if they are capable of transmitting infectious agents.**

Store all samples at specified temperatures.
Sample stability is affected by elevated temperatures.
Always use caution when transferring specimens from a primary collection tube to a secondary tube.
Use pipettes with aerosol-barrier or positive-displacement tips to handle specimens.
Always use a new pipette tip for each specimen.
Ensure samples are equilibrated to room temperature prior to transfer into a secondary tube.

## Sample collection

Table 10 summarizes what collection devices can be used with specific sample types.

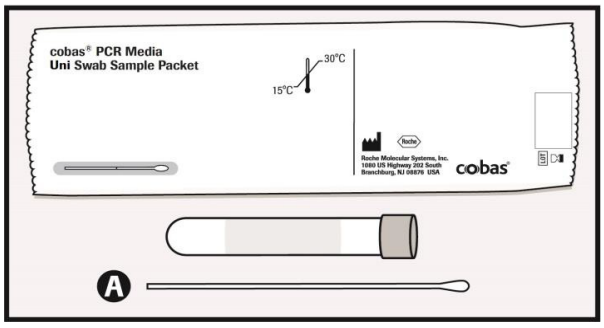
**Table 10** Overview of collection devices and sample types

| Collection Device | Nasopharyngeal | Nasal |
|---|---|---|
| Copan Universal Transport Media (UTM-RT®) | √ | √ |
| BD™ Universal Viral Transport (UVT) | √ | √ |
| 0.9% Physiological saline | | √ |
| cobas® PCR Media Uni Swab Sample Kit | | √ |
| cobas® PCR Media Dual Swab Sample Kit | | √ |
| cobas® PCR Media Kit (and 100 Tube PCR Media Kit) | | √ |

- Collect nasal and nasopharyngeal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place in 3 mL of Copan Universal Transport Medium (UTM-RT®) or BD™ Universal Viral Transport (UVT) or equivalent.
- Collect nasal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place into cobas® PCR Media tube from cobas® PCR Media Kit (P/N 06466281190).
- Collect nasal specimens using the cobas® PCR Media Uni Swab Sample Kit (P/N 07958030190) or cobas® PCR Media Dual Swab Sample Kit (P/N 07958021190) according to instructions below
- Refer to the Instructions for Use of the Collection Devices for hazard information.

## Nasal (anterior nares) swab specimen collection - healthcare worker or self-collected on site

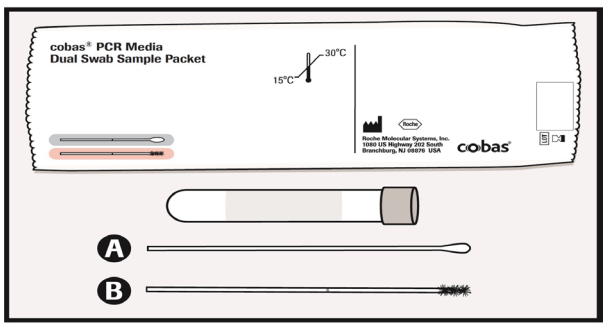
## WARNING: DO NOT PREWET SWAB IN cobas® PCR MEDIA BEFORE COLLECTION!




The cobas® PCR Media Uni Swab Sample kit contains:

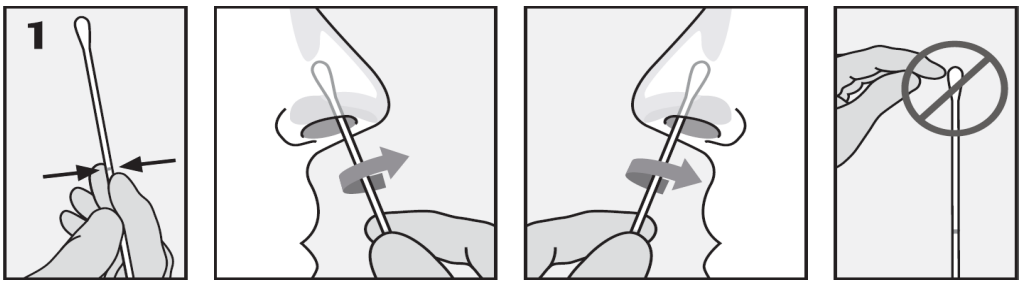
cobas® PCR Media Tube
Woven Swab: A

OR




The cobas® PCR Media Dual Swab Sample kit contains:

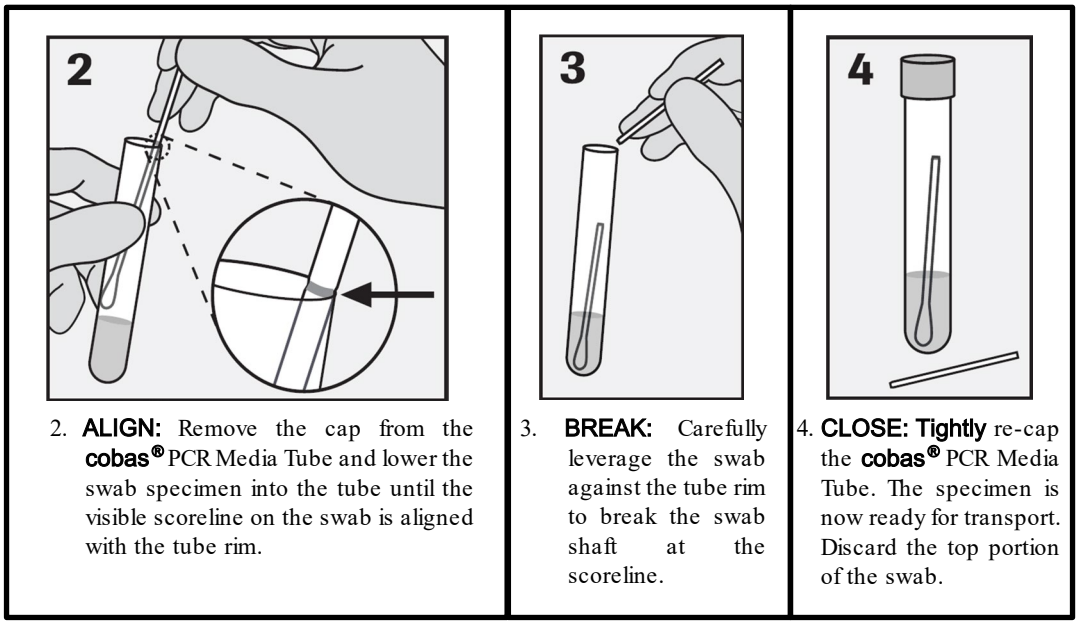
cobas® PCR Media Tube
Woven Swab: A
Flocked Swab: B




**DO NOT PREWET SWAB IN cobas® PCR MEDIA BEFORE COLLECTION!**

1. **COLLECT:** Hold the woven swab (Swab A) or the flocked swab (Swab B) with the scoreline above your hand. Insert the swab 1-2 cm into one of the anterior nares. Rotate the swab against the nasal mucosa for about 3 seconds and withdraw. Repeat with the other anterior nare using the same swab.

   Do not let the swab touch any surface before placing it into the collection tube.




2. **ALIGN:** Remove the cap from the cobas® PCR Media Tube and lower the swab specimen into the tube until the visible scoreline on the swab is aligned with the tube rim.
3. **BREAK:** Carefully leverage the swab against the tube rim to break the swab shaft at the scoreline.
4. **CLOSE: Tightly** re-cap the cobas® PCR Media Tube. The specimen is now ready for transport. Discard the top portion of the swab.

- Collect nasal specimens according to standard collection technique using flocked or polyester-tipped swabs and immediately place in 3 mL of 0.9% physiological saline.

## Transport and storage

- Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents.
- Samples collected in UTM-RT®
  - After collection, specimens can be stored for up to 48 hours at 2-25°C followed by up to 3 days at 2-8°C.
- Samples collected in cobas® PCR Media
  - After collection, specimens can be stored for up to 24 hours at 2-25°C followed by up to 3 days at 2-8°C.
- Samples collected in 0.9% physiological saline
  - After collection, specimens can be stored for up to 48 hours at 2-25°C followed by up to 3 days at 2-8°C.
- If delivery and processing of samples exceeds specified time periods, specimens should be transported in dry ice and once in laboratory frozen at -70°C or colder

# Instructions for use

## Procedural notes

- Do not use cobas® SARS-CoV-2 & Influenza A/B v2 reagents, cobas® SARS-CoV-2 & Influenza A/B Control Kit, cobas® Buffer Negative Control Kit, or cobas® omni reagents after their expiry dates.
- Do not reuse consumables. They are for one-time use only.
- Ensure that specimen barcode labels on sample tubes are visible through the openings on the side of the samp racks. Refer to the cobas® 6800/8800 Systems User Guide for proper barcode specifications and additional information on loading sample tubes.
- Refer to the cobas® 6800/8800 Systems User Assistance and/or User Guide for proper maintenance of instruments.

## Running cobas® SARS-CoV-2 & Influenza A/B v2

cobas® SARS-CoV-2 & Influenza A/B v2 can be run with a minimum required sample volume of 0.6 mL in the cobas® omni Secondary Tube for specimens collected in an Universal Transport Medium (UTM-RT®), BD™ Universal Viral Transport (UVT), cobas® PCR Media or 0.9% physiological saline. Specimens collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kit can be run in their primary collection tube with a minimum required sample volume of 1.0 mL.

### Specimens collected in cobas® PCR Media, 0.9% physiological saline, UTM-RT® or UVT

Specimens collected in tubes compatible with cobas® 6800/8800 Systems may be loaded directly onto the cobas® 6800/8800 Systems. The swab must be removed from the sample tube prior to direct loading onto the system. Specimens collected in tubes which are not compatible with the cobas® 6800/8800 Systems must be transferred into a secondary tube prior to processing on the cobas® 6800/8800 Systems. The cobas® omni Secondary Tube is the preferred option. If using frozen samples in secondary tubes, place the samples at room temperature (15-30°C) until completely thawed and then briefly mix (e.g., vortex for 3-5 seconds) and centrifuge to collect all sample volume at the bottom of the tube. Samples should be processed using the sample type selection in the user interface (UI) as described in Table 11. Additional tubes for testing cobas® SARS-CoV-2 & Influenza A/B v2 are available. Contact your local Roche representative for detailed testing instructions and an order list of primary tubes and secondary tubes compatible with the instruments.

Follow the steps below to transfer patient sample from a primary collection tube into a cobas® omni Secondary Tube:

- Unscrew the primary sample tube cap.
- Lift the cap and any attached swab to allow a pipette to be inserted into the sample tube.
- Transfer at least 0.6 mL into the prepared barcoded secondary tube.
- Transfer secondary tube to a rack. Close the primary sample tube cap.

## Specimens collected using cobas® PCR Media Uni or Dual Swab Sample Kit

Samples collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kit must be uncapped and can be loaded directly onto racks for processing on cobas® 6800/8800 Systems. Transfer into a secondary tube is not necessary. cobas® PCR Media tubes fit on to the MPA RACK 16 MM and can be processed with the swab remaining in the tube. Samples collected using cobas® PCR Media Uni Swab Sample Kit or cobas® PCR Media Dual Swab Sample Kits should be processed using the cobas® PCR Media swab sample type selection in the user interface (UI) of the cobas® SARS-CoV-2 & Influenza A/B v2 as described in Table 11.

A properly collected swab specimen should have a single swab with the shaft broken at the scoreline. Swab shafts which are broken above the score line will appear longer than normal and may also be bent over to fit into the cobas® PCR Media tube. This may create an obstruction to the pipetting system which can cause the loss of sample, test results and/or mechanical damage to the instrument. In the event that a swab specimen has an improperly broken shaft, remove the swab prior to sample processing on the cobas® 6800/8800 Systems. Use caution when disposing of specimen swabs; avoid splashing or touching swabs to other surfaces during disposal to prevent contamination.

Incoming cobas® PCR Media primary swab specimen tubes with no swabs or with two swabs have not been collected according to the instructions in their respective collection kit IFU and should not be tested. If the sample containing two swabs in the cobas® PCR Media primary tubes must be tested, transfer 0.6 mL into the prepared barcoded secondary tube.

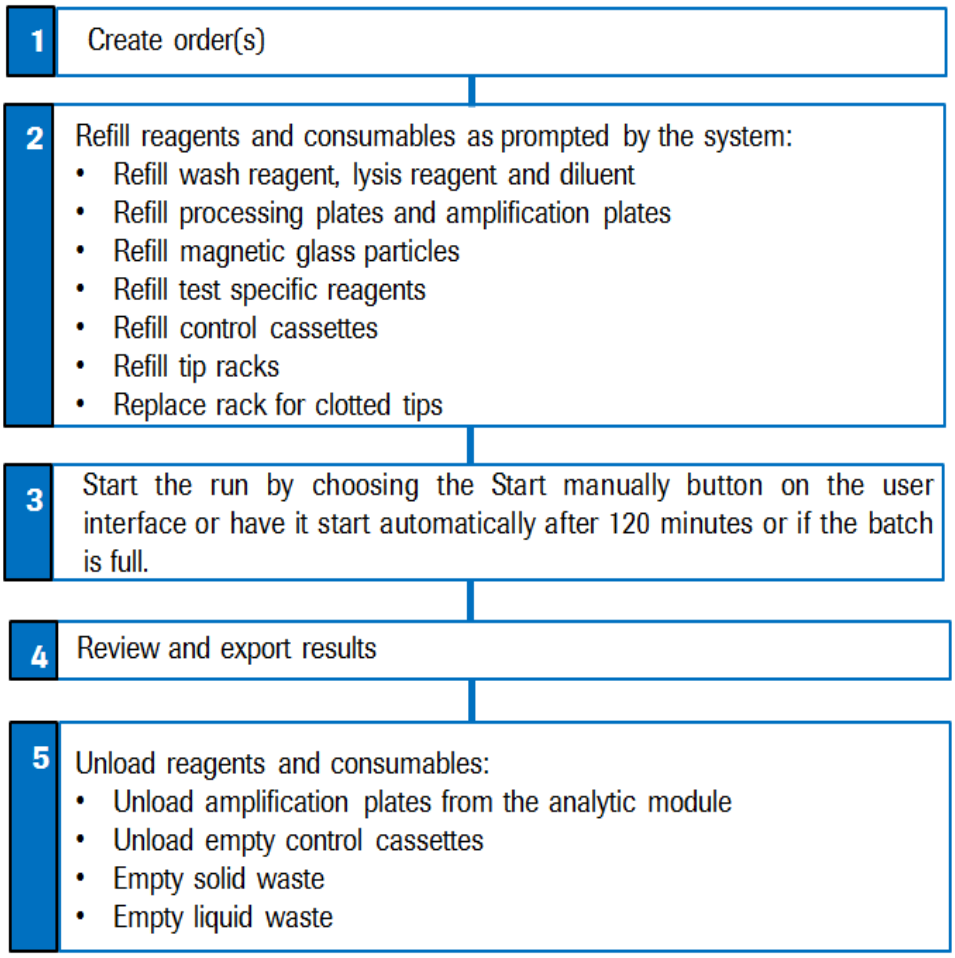
Occasionally, incoming swab specimens contain excessive mucus which may induce a pipetting error (e.g., clot or other obstruction) on the cobas® 6800/8800 Systems. Prior to retesting of specimens that exhibited clots during initial processing, remove and discard the swab, then recap and vortex these specimens for 30 seconds to disperse the excess mucus. Swab specimens can be processed twice on the cobas® 6800/8800 Systems while the swab is in the collection tube. If additional testing is required, or if the first test fails due to specimen pipetting error (e.g., clot or other obstruction), the swab must be removed and the remaining fluid must have a minimum volume of 1.0 mL. The test procedure is described in detail in the cobas® 6800/8800 Systems - User Assistance and/or User Guide. Figure 1 below summarizes the procedure.

**Table 11** Sample type selection in the user interface of the cobas® SARS-CoV-2 & Influenza A/B v2

| Collection kit /Matrix type | Minimum volume (mL) Processing tube | Process as Sample Type |
|---|---|---|
| Copan Universal Transport Medium (UTM-RT®)<br>BD™ Universal Viral Transport<br>0.9% Physiological saline<br>cobas® PCR Media Kit | 0.6 mL<br>cobas® omni Secondary tube | VTM |
| Copan Universal Transport Medium (UTM-RT®)<br>BD™ Universal Viral Transport<br>0.9% Physiological saline<br>cobas® PCR Media Kit | Compatible tubes without swab inside the tube; for dead volume contact your local Roche representative | VTM |
| cobas® PCR Media Uni or Dual Swab Sample Kit | 1.0 mL<br>Primary tube | cobas® PCR Media swab |

The test procedure is described in detail in the cobas® 8800/8800 System User Assistance and/or User Guide. Figure 1 below summarizes the procedure.

**Figure 1** cobas® SARS-CoV-2 & Influenza A/B v2 procedure



# Results

The cobas® 6800/8800 Systems automatically detects the SARS-CoV-2, influenza A and influenza B, for each individually processed sample and control, displaying individual target results for samples as well as test validity and overall results for controls.

## Quality control and validity of results

- One cobas® Buffer Negative Control [BUF (-) C] and one [SCoV2-FluA/B CTL] are processed with each batch.
- In the cobas® 6800/8800 software and/or report, check for flags and their associated results to ensure the batch validity.
- All flags are described in the cobas® 6800/8800 Systems User Guide.
- The batch is valid if no flags appear for any controls. If the batch is invalid, repeat testing of the entire batch.

Validation of results is performed automatically by the cobas® 6800/8800 software based on negative and positive control performance.

## Interpretation of results on the cobas ® 6800/8800 Systems

Display examples for cobas® SARS-CoV-2 & Influenza A/B v2 are shown in Figure 2.

**Figure 2** Example of **cobas®** SARS-CoV-2 & Influenza A/B v2 results display on the **cobas®** 6800/8800 System

| Test | Sample ID | Valid* | Flags | Sample type | Overall result* | Target 1 | Target 2 | Target 3 | Target 4 |
|---|---|---|---|---|---|---|---|---|---|
| SCoV2-FluA/B 400 µL | Sample_01 | NA | | VTM | **NA** | FluA Negative | SCoV2 Negative | PanSarb Negative | FluB Negative |
| SCoV2-FluA/B 400 µL | Sample _02 | NA | Y40T | VTM | **NA** | Invalid | Invalid | Invalid | Invalid |
| SCoV2-FluA/B 400 µL | Sample _03 | NA | | VTM | **NA** | FluA Positive | SCoV2 Negative | PanSarb Negative | FluB Negative |
| SCoV2-FluA/B 400 µL | Sample _04 | NA | | VTM | **NA** | FluA Negative | SCoV2 Positive | PanSarb Positive | FluB Negative |
| SCoV2-FluA/B 400 µL | Sample _05 | NA | | VTM | **NA** | FluA Negative | SCoV2 Negative | PanSarb Negative | FluB Positive |
| SCoV2-FluA/B 400 µL | Sample _06 | NA | | VTM | **NA** | FluA Negative | SCoV2 Negative | PanSarb Positive | FluB Negative |
| SCoV2-FluA/B 400 µL | Sample _07 | NA | C01H2 | VTM | **NA** | FluA Positive | Invalid | Invalid | Invalid |
| SCoV2-FluA/B 400 µL | Sample _08 | NA | C01H1 | VTM | **NA** | Invalid | SCoV2 Positive | Invalid | FluB Positive |
| SCoV2-FluA/B | C161420284090428828404 | Yes | | (-) Ctrl | **Valid** | Valid | Valid | Valid | Valid |
| SCoV2-FluA/B | C161420284093009580264 | Yes | | SCoV2-FluA/B (+) C | **Valid** | Valid | Valid | Valid | Valid |

*The "Valid" and "Overall Result" columns are not applicable to sample results for **cobas®** SARS-CoV-2 & Influenza A/B v2. Values reported in these columns are not applicable and do not impact the validity of results reported within individual target result columns. Refer to Table 12, **cobas®** SARS-CoV-2 & Influenza A/B v2 results interpretation for specific instructions on test results interpretation.

## Interpretation of results

For a valid batch, check each individual sample for flags in the **cobas®** 6800/8800 software and/or report. The result interpretation should be as follows:

- A valid batch may include both valid and invalid sample results.
- Invalid results for one or more target combinations are possible and are reported out specifically for each channel.
- Results of this test should only be interpreted in conjunction with information available from clinical evaluation of the patient and patient history.

Results and their corresponding interpretation for detecting SARS-CoV-2 & Influenza A/B are shown below (Table 12).

**Table 12 cobas®** SARS-CoV-2 & Influenza A/B v2 results interpretation

| Target 1 Influenza A* | Target 2 SARS-CoV-2 | Target 3 Pan-Sarbecovirus | Target 4 Influenza B* | Interpretation |
|---|---|---|---|---|
| Negative | Negative | Negative | Negative | No target RNA Detected |
| Negative | Negative | Negative | Positive | Influenza B RNA Detected |
| Positive | Negative | Negative | Negative | Influenza A RNA Detected |
| Positive | Negative | Negative | Positive | Influenza A and Influenza B RNA Detected |

| Target 1 Influenza A* | Target 2 SARS-CoV-2 | Target 3 Pan-Sarbecovirus | Target 4 Influenza B* | Interpretation |
|---|---|---|---|---|
| Negative | Negative | Positive | Negative | Presumptive Positive for SARS-CoV-2 RNA. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management. |
| Negative | Negative | Positive | Positive | Presumptive Positive for SARS-CoV-2 RNA and influenza B RNA Detected. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management. |
| Positive | Negative | Positive | Negative | Influenza A RNA Detected and Presumptive Positive for SARS-CoV-2 RNA. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management. |

| Target 1 Influenza A* | Target 2 SARS-CoV-2 | Target 3 Pan-Sarbecovirus | Target 4 Influenza B* | Interpretation |
|---|---|---|---|---|
| Positive | Negative | Positive | Positive | Influenza A RNA Detected, Presumptive Positive for SARS-CoV-2 RNA, and influenza B RNA Detected. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors.<br>For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management. |
| Negative | Positive | Negative | Negative | SARS-CoV-2 RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors. |
| Negative | Positive | Negative | Positive | SARS-CoV-2 RNA and influenza B RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors. |
| Positive | Positive | Negative | Negative | Influenza A RNA and SARS-CoV-2 RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors. |
| Positive | Positive | Negative | Positive | Influenza A RNA, SARS-CoV-2 RNA, and influenza B RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors. |
| Negative | Positive | Positive | Negative | SARS-CoV-2 RNA Detected |
| Negative | Positive | Positive | Positive | SARS-CoV-2 RNA and influenza B RNA Detected |
| Positive | Positive | Positive | Negative | Influenza A RNA and SARS-CoV-2 RNA Detected |
| Positive | Positive | Positive | Positive | Influenza A RNA, SARS-CoV-2 RNA, and influenza B RNA Detected |

If any individual target result is invalid, the presence or absence of that individual target cannot be determined. Other initial valid target results can be interpreted as described in the table.

*Results (positive and negative) for influenza should be interpreted with caution. If an influenza result is inconsistent with clinical presentation and/or other clinical and epidemiological information, FDA-cleared influenza NAATs are available for confirmation if clinically indicated.

## Procedural limitations

- cobas® SARS-CoV-2 & Influenza A/B v2 has been evaluated only for use in combination with the cobas® SARS-CoV-2 & Influenza A/B Control Kit, cobas® Buffer Negative Control Kit, cobas® omni MGP Reagent, cobas® omni Lysis Reagent, cobas® omni Specimen Diluent, and cobas® omni Wash Reagent for use on the cobas® 6800/8800 Systems.
- Reliable results depend on proper sample collection, storage and handling procedures.
- This test is intended to be used for the detection of SARS-CoV-2, influenza A, and influenza B RNA in nasopharyngeal and nasal swab samples collected in Copan Universal Transport Medium (UTM-RT®) or BD™ Universal Viral Transport System (UVT), and nasal swab samples collected in cobas® PCR Media and 0.9% physiological saline. Testing of other sample types with cobas® SARS-CoV-2 & Influenza A/B v2 may result in inaccurate results
- Detection of SARS-CoV-2 and influenza A/B RNA may be affected by sample collection methods, patient factors (e.g, presence of symptoms), and/or stage of infection.
- As with any molecular test, mutations within the target regions of cobas® SARS-CoV-2 & Influenza A/B v2 could affect primer and/or probe binding resulting in failure to detect the presence of virus.
- Due to inherent differences between technologies, it is recommended that, prior to switching from one technology to the next, users perform method correlation studies in their laboratory to qualify technology differences. One hundred percent agreement between the results should not be expected due to aforementioned differences between technologies. Users should follow their own specific policies/procedures.
- False negative or invalid results may occur due to interference. The Internal Control is included in cobas® SARS-CoV-2 & Influenza A/B v2 to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification.
- The addition of AmpErase enzyme into the cobas® SARS-CoV-2 & Influenza A/B v2 Master Mix reagent enables selective amplification of target RNA; however, good laboratory practices and careful adherence to the procedures specified in this Instructions For Use document are necessary to avoid contamination of reagents.
- Results (positive and negative) for influenza should be interpreted with caution. If an influenza result is inconsistent with clinical presentation and/or other clinical and epidemiological information, FDA-cleared influenza NAATs are available for confirmation if clinically indicated.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. The 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 and their prevalence, which change over time.

## Conditions of Authorizations for Labs

cobas® SARS-CoV-2 & Influenza A/B v2 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/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas

However, to assist clinical laboratories using cobas® SARS-CoV-2 & Influenza A/B v2 ("this product" in the conditions below), the relevant Conditions of Authorization are listed below:

A. Authorized laboratories using this product[1] 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.
B. Authorized laboratories using this product must use this product 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 this product are not permitted.
C. Authorized laboratories that receive this product must notify the relevant public health authorities of their intent to run this product prior to initiating testing.
D. Authorized laboratories using this product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
E. Authorized laboratories must collect information on the performance of this product and report to DMD/OHT7/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Roche Diagnostics US Customer Technical Support (via telephone number 1-800-526-1247) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of this product of which they become aware.
F. All laboratory personnel using this product must be appropriately trained in real time RT-PCR techniques and instruments used in the cobas® SARS-CoV-2 & Influenza A/B v2, and use appropriate laboratory and personal protective equipment when handling this kit, and use this product in accordance with the authorized labeling.
G. Roche Molecular Systems, authorized distributor(s) and authorized laboratories using this product 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.

[1] "This product" refers to cobas® SARS-CoV-2 & Influenza A/B v2. The letter of authorization refers to, "Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests" as "authorized laboratories."

# Non-clinical performance evaluation

cobas® SARS-CoV-2 & Influenza A/B v2 is an updated version of cobas® SARS-CoV-2 & Influenza A/B comprised of an influenza A dual target assay design which improves inclusivity of the test. The influenza B and SARS-CoV-2 targeting assays of cobas® SARS-CoV-2 & Influenza A/B remained unchanged on cobas® SARS-CoV-2 & Influenza A/B v2.

Studies were conducted to demonstrate that the general performance of each target of the assay is unchanged and to demonstrate the effectiveness of the updated design of the influenza A target. The following key performance characteristics data were regenerated with either cobas® SARS-CoV-2 & Influenza A/B or cobas® SARS-CoV-2 & Influenza A/B v2.

## Key performance characteristics

### Analytical sensitivity (Limit of Detection)

The Limit of Detection (LoD) study determines the lowest detectable concentration of SARS-CoV-2, influenza A, and influenza B at which greater or equal to 95% of all (true positive) replicates test positive.

To determine the LoD, six cultured viruses – two each of influenza A and influenza B strains as well as the live and the heat-inactivated form of SARS-CoV-2 isolate from a US patient – were serially diluted in simulated clinical matrix to build two co-formulated target panels and three target single-formulated panels with one strain per virus. Seven to eight concentration levels, with two-fold serial dilutions between the levels, were prepared on three days and tested with a total of 63 replicates per concentration across three reagent lots for co-formulated panels and with a total of 21 replicates per concentration using one reagent lot for single-formulated panels. Table 13 to Table 16 summarize the established LoD values.

**Table 13** Summary of LoD for influenza A determined with cobas® SARS-CoV-2 & Influenza A/B*

| Viral Strain | Kit lot | Panel | 95% Probit [$TCID_{50}$/mL] | 95% CI of Probit [$TCID_{50}$/mL] | Hit rate ⩾95% [$TCID_{50}$/mL] | Mean Ct at ⩾95% Hit rate |
|---|---|---|---|---|---|---|
| A/Kansas/14/2017 (H3N2)** Cat No 0810586CF Lot 323540 | Lot 1 | single-formulated | **0.050** | 0.034 – 0.098 | **0.036** | 38.2 |
| | Lot 1 | co-formulated | **0.12** | 0.073 – 0.28 | **0.071** | 36.6 |
| | Lot 2 | co-formulated | **0.083** | 0.054 – 0.17 | **0.14** | 36.7 |
| | Lot 3 | co-formulated | **0.062** | 0.040 – 0.14 | **0.071** | 37.0 |
| | Lot 1-3 | co-formulated | **0.086** | 0.065 – 0.12 | **0.071** | 37.5 |
| A/Brisbane/02/2018 (H1N1)*** Cat No 0810585CF Lot 323771 | Lot 1 | co-formulated | **0.020**** | 0.013 – 0.048 | **0.026** | 37.4 |
| | Lot 2 | co-formulated | **0.020** | 0.013 – 0.064 | **0.026** | 38.4 |
| | Lot 3 | co-formulated | **0.025** | 0.016 – 0.059 | **0.026** | 38.1 |
| | Lot 1-3 | co-formulated | **0.022** | 0.017 – 0.034 | **0.026** | 38.0 |

* LoD equivalency was demonstrated via performance studies with cobas® SARS-CoV-2 & Influenza A/B v2, refer to Table 17.

** Lot specific factor to convert $TCID_{50}$ into copy number was determined using NATrol™ Influenza A H3 Stock (Catalog# NATFLUAH3-STQ, Lot: 331079) material. 1 $TCID_{50}$/mL corresponds to 631 cp/mL.

*** Lot specific factor to convert $TCID_{50}$ into copy number was determined using NATrol™ Influenza A H1 Stock (Catalog# NATFLUAH1-STQ, Lot: 331080) material. 1 TCID50/mL corresponds to 5811 cp/mL.

**** Claimed LoD was verified testing influenza A H1N1pdm09 strains containing the C124A (GISAID: EPI_ISL_14387941), and the C124A plus G141A mutations in the M gene (GISAID: EPI_ISL_15803829) with cobas® SARS-CoV-2 & Influenza A/B v2.

**Table 14** Summary of LoD for influenza B determined with **cobas®** SARS-CoV-2 & Influenza A/B*

| Viral Strain | Kit lot | Panel | 95% Probit [$TCID_{50}$/mL] | 95% CI of Probit [$TCID_{50}$/mL] | Hit rate ⩾95% [$TCID_{50}$/mL] | Mean Ct at ⩾95% Hit rate |
|---|---|---|---|---|---|---|
| B/Phuket/3073/2013 (Yamagata lineage) Cat No 0810515CF Lot 320436 | Lot 1 | single-formulated | **0.011** | 0.0076 – 0.023 | **0.017** | 35.4 |
| | Lot 1 | co-formulated | **0.019** | 0.012 – 0.044 | **0.034** | 35.1 |
| | Lot 2 | co-formulated | **0.016** | 0.0095 – 0.050 | **0.017** | 35.4 |
| | Lot 3 | co-formulated | **0.019** | 0.010 – 0.084 | **0.017** | 35.3 |
| | Lot 1-3 | co-formulated | **0.017** | 0.012 – 0.026 | **0.017** | 35.3 |
| B/Colorado/06/2017 (Victoria lineage) Cat No 0810573CF Lot 323459 | Lot 1 | co-formulated | **0.027** | 0.017 – 0.065 | **0.026** | 34.9 |
| | Lot 2 | co-formulated | **0.032** | 0.019 – 0.084 | **0.053** | 34.5 |
| | Lot 3 | co-formulated | **0.019** | 0.012 – 0.050 | **0.026** | 35.0 |
| | Lot 1-3 | co-formulated | **0.026** | 0.019 – 0.040 | **0.026** | 34.9 |

*LoD equivalency was demonstrated via performance with the **cobas®** SARS-CoV-2 & Influenza A/B 2, refer to Table 17.

**Table 15** Summary of LoD for SARS-CoV-2 determined with **cobas®** SARS-CoV-2 & Influenza A/B*

| Viral Strain | Kit lot | Panel | 95% Probit [$TCID_{50}$/mL] | 95% CI of Probit [$TCID_{50}$/mL] | Hit rate ⩾95% [$TCID_{50}$/mL] | Mean Ct at ⩾95% Hit rate |
|---|---|---|---|---|---|---|
| USA-WA1/2020 heat-inactivated Cat No 0810587CFHI Lot 324045 | Lot 1 | single-formulated | **0.068** | 0.044 – 0.15 | **0.058** | 36.9 |
| | Lot 1 | co-formulated | **0.14** | 0.086 – 0.35 | **0.12** | 36.3 |
| | Lot 2 | co-formulated | **0.13** | 0.083 – 0.26 | **0.12** | 36.4 |
| | Lot 3 | co-formulated | **0.10** | 0.065 – 0.25 | **0.12** | 35.9 |
| | Lot 1-3 | co-formulated | **0.13** | 0.094 – 0.19 | **0.12** | 36.2 |
| USA-WA1/2020 infectious culture Cat No NR-52281 Lot 70033175** | Lot 1 | co-formulated | **0.0081** | 0.0041 – 0.049 | **0.0079** | 36.2 |
| | Lot 2 | co-formulated | **0.0071** | 0.0044 – 0.018 | **0.0079** | 36.2 |
| | Lot 3 | co-formulated | **0.0052** | 0.0032 – 0.013 | **0.0079** | 35.9 |
| | Lot 1-3 | co-formulated | **0.0063** | 0.0046 – 0.010 | **0.0079** | 36.1 |

* LoD equivalency was demonstrated via performance with the **cobas®** SARS-CoV-2 & Influenza A/B 2, refer to Table 17.

**Based on the information provided in the Certificate of Analysis from the vendor, 1 $TCID_{50}$/mL is equal to 7,393 genome equivalents/mL by dPCR.

**Table 16** Summary of LoD for pan-Sarbecovirus determined with cobas® SARS-CoV-2 & Influenza A/B*

| Viral Strain | Kit lot | Panel | 95% Probit [$TCID_{50}$/mL] | 95% CI of Probit [$TCID_{50}$/mL] | Hit rate ⩾95% [$TCID_{50}$/mL] | Mean Ct at ⩾95% Hit rate |
|---|---|---|---|---|---|---|
| USA-WA1/2020 heat-inactivated Cat No 0810587CFHI Lot 324045 | Lot 1 | single-formulated | **0.14** | 0.08 – 0.37 | **0.12** | 35.6 |
| | Lot 1 | co-formulated | **0.28** | 0.17 – 0.67 | **0.55** | 34.5 |
| | Lot 2 | co-formulated | **0.23** | 0.14 – 0.49 | **0.23** | 35.1 |
| | Lot 3 | co-formulated | **0.18** | 0.11 – 0.37 | **0.23** | 34.8 |
| | Lot 1-3 | co-formulated | **0.23** | 0.17 – 0.34 | **0.55** | 34.2 |
| USA-WA1/2020 infectious culture Cat No NR-52281 Lot 70033175** | Lot 1 | co-formulated | **0.0090** | 0.0057 – 0.020 | **0.016** | 34.6 |
| | Lot 2 | co-formulated | **0.0076** | 0.0049 – 0.016 | **0.016** | 34.7 |
| | Lot 3 | co-formulated | **0.0080** | 0.0053 – 0.017 | **0.0079** | 35.3 |
| | Lot 1-3 | co-formulated | **0.0082** | 0.0062 – 0.012 | **0.016** | 34.7 |

* LoD equivalency was demonstrated via performance with the cobas® SARS-CoV-2 & Influenza A/B v2, refer to Table 17

**Based on the information provided in the Certificate of Analysis from the vendor, 1 $TCID_{50}$/mL is equal to 7,393 genome equivalents by ddPCR.

## LoD Equivalency

In order to show LoD equivalency of cobas® SARS-CoV-2 & Influenza A/B v2 compared to the previous version, the cobas® SARS-CoV-2 & Influenza A/B, a co-formulated panel, consisting of influenza A, influenza B and SARS-CoV-2, was tested with 21 replicates per panel member and assay version to compare the LoD in simulated clinical matrix in Universal Transport Media (UTM™). One reagent lot was used of each assay version. The summary of the results is shown in Table 17.

**Table 17** LoD Equivalency between cobas® SARS-CoV-2 & Influenza A/B and cobas® SARS-CoV-2 & Influenza A/B v2

| Target | Viral Strain | cobas® SARS-CoV-2 & Influenza A/B 95% Probit ($TCID_{50}$/mL) | cobas® SARS-CoV-2 & Influenza A/B v2 95% Probit Predicted 95% ($TCID_{50}$/mL) | cobas® SARS-CoV-2 & Influenza A/B Lower 95% to Upper 95% Confidence Interval ($TCID_{50}$/mL) | cobas® SARS-CoV-2 & Influenza A/B v2 Lower 95% to Upper 95% Confidence Interval ($TCID_{50}$/mL) |
|---|---|---|---|---|---|
| Influenza A | A/Kansas/14/2017 (H3N2) Cat No 0810586CF Lot 323540 | 0.077 | 0.040 | 0.047- 0.190 | 0.026- 0.088 |
| SARS-CoV-2 | USA-WA1/2020 heat-inactivated Cat No 0810587CFHI Lot 324045 | 0.124 | 0.053 | 0.077- 0.296 | 0.036- 0.116 |
| Pan Sarbecovirus | | 0.173 | 0.078 | 0.112- 0.356 | 0.005- 0.156 |
| Influenza B | Phuket/3073/2013 (Yamagata lineage) Cat No 0810515CF Lot 320436 | 0.023 | 0.011 | 0.014- 0.057 | 0.007- 0.026 |

## Inclusivity

The inclusivity for the detection of influenza A was confirmed by testing thirteen influenza A strains with cobas® SARS-CoV-2 & Influenza A/B v2. All strains tested showed 100% hit rate at the concentrations indicated in Table 18.

**Table 18** Summary of inclusivity for influenza A tested with cobas® SARS-CoV-2 & Influenza A/B v2

| Viral Target | Strain | Catalog Number | Concentration |
|---|---|---|---|
| Influenza A | A/Canada/6294/09 (H1N1) | 0810109CFJ | 1.60E-02 $TCID_{50}$/mL |
| | A/California/07/09 (H1N1) | 0810165CF | 2.31E-01 $TCID_{50}$/mL |
| | A/Mexico/4108/09 (H1N1) | 0810166CF | 8.71E-02 $TCID_{50}$/mL |
| | A/Singapore/63/04 (H1N1) | 0810246CF | 1.69E-02 $TCID_{50}$/mL |
| | A/Michigan/45/15 (H1N1) | 0810538CF | 9.28E-02 $TCID_{50}$/mL |
| | A/California/04/09(H1N1) | VR-1805 | 6.41E+00 $TCID_{50}$/mL |
| | A/England/224020815/2022(H1N1)* | n/a | 4.52E+02 cp/mL*** |
| | A/England/221740513/2022(H1N1)** | n/a | 4.52E+02 cp/mL*** |
| | A/Perth/16/09 (H3N2) | 0810251CF | 6.30E-02 $TCID_{50}$/mL |
| | A/Wisconsin/67/05 (H3N2) | 0810252CF | 4.37E-01 $TCID_{50}$/mL |
| | A/Switzerland/9715293/13 (H3N2) | 0810511CF | 3.63E-02 $TCID_{50}$/mL |
| | A/HongKong/4801/14 (H3N2) | 0810526CF | 3.57E-01 $TCID_{50}$/mL |
| | A/Texas/50/12 (H3N2) | 0810238CF | 2.7E+00 $TCID_{50}$/mL |

* GISAID ID EPI_ISL_15803829 containing the C124A and G141A mutations in the N gene (Strain is not commercially available)
** GISAID ID EPI_ISL_14387941 containing the C124A mutation in the M gene (Strain is not commercially available)
***Copy number was determined using AccuPlex™ Influenza A H1 Stock (Catalog# NATFLUAH1-STQ, Lot: 331030) as material

The inclusivity for the detection of influenza B and SARS-CoV-2 was confirmed by testing five influenza B and three SARS-CoV-2 strains with cobas® SARS-CoV-2 & Influenza A/B. The lowest target analyte at which all four tested replicates were positive are reported (Table 19 and Table 20).

**Table 19** Summary of inclusivity influenza B tested with cobas® SARS-CoV-2 & Influenza A/B

| Viral Target | Strain | Catalog Number | Lot Number | Lowest Concentration Detected |
|---|---|---|---|---|
| Influenza B | B/Brisbane/60/2008 (Victoria lineage) | 0810254CF | 313257 (sublot: 513438) | 0.002 $TCID_{50}$/mL |
| | B/Utah/9/14 (Yamagata lineage) | 0810516CF | 317295 (sublot: 527062) | 0.017 $TCID_{50}$/mL |
| | B/Alabama/2/17 (Victoria lineage) | 0810572CF | 322548 | 0.0064 $TCID_{50}$/mL |
| | B/Florida/78/2015 (Victoria Lineage) | VR-1931 | 70020870 | 0.076 $TCID_{50}$/mL |
| | B/Wisconsin/1/2010 (Yamagata Lineage) | VR-1883 | 70012127 | 0.070 $CEID_{50}$/mL |

**Table 20** Summary of inclusivity for SARS-CoV-2 tested with cobas® SARS-CoV-2 & Influenza A/B

| Viral Target | Strain | Catalog Number | Lot Number | Lowest Concentration Detected |
|---|---|---|---|---|
| SARS-CoV-2 | BetaCoV/France/IDF0372/2020 | 014V-03890 | Not available | 0.038 PFU/mL |
| | BetaCoV/Munich/BavPat1/2020 | 026V-03883 | Not available | 0.0036 PFU/mL |
| | 2019-nCoV/Italy-INMI1 | 008V-03893 | Not available | 0.062 $TCID_{50}$/mL |

Further, cobas® SARS-CoV-2 & Influenza A/B was shown to be inclusive for the CDC Human Influenza Virus Panel (2020) (Cat. Number VP2020, Lot Number 200330). The lowest concentration where at least one out of five replicates was positive is reported as the minimum reactive concentration in Table 21.

**Table 21** Summary of CDC Human Influenza Virus Panel (2020) tested with cobas® SARS-CoV-2 & Influenza A/B

| Virus | Strain | Minimum Reactive Concentration [$EID_{50}$/mL] |
|---|---|---|
| Influenza A | A/Perth/16/2009 (H3N2) | 2.62E+00 |
| | A/Hong Kong/2671/2019 (H3N2) | 8.29E+02 |
| | A/Christ Church/16/2010 (H1N1 pdm) | 2.08E+01 |
| | A/Guangdong-maonan/1536/2019 (H1N1 pdm) | 6.00E+01 |
| Influenza B | B/Michigan/09/2011 | 1.30E+02 |
| | B/Washington/02/2019 | 2.08E+00 |
| | B/Texas/81/2016 | 6.54E+02 |
| | B/Phuket/3073/2013 | 2.08E+01 |

## Precision ( repeatability )

Within-laboratory precision was examined using a panel composed of spiked influenza A (A/Kansas/14/2017), influenza B (B/Phuket/3073/2013) and SARS-CoV-2 (USA-WA1/2020, heat-inactivated) cultures diluted in simulated clinical matrix in UTM-RT®. Sources of variability were examined with a panel consisting of three concentration levels, using three lots of cobas® SARS-CoV-2 & Influenza A/B reagents and two instruments over a time course of 15 days for a total of 30 runs. A description of the precision panel and the observed positivity rates are shown in Table 22. All negative panel members tested negative throughout the study. Analysis of standard deviation and percent coefficient of variation (%CV) of the Ct values from tests performed on positive panel members (see Table 23) yielded overall CV percentages ranging from 1.2% to 5.1% for influenza A, influenza B, and SARS-CoV-2.

**Table 22** Summary of within laboratory precision

| Target Concentration | N Tested | N Positive | Positivity Rate | 95% Confidence Interval | |
|---|---|---|---|---|---|
| | | | | Lower Limit | Upper Limit |
| **Influenza A** | | | | | |
| Negative | 90 | 0 | 0% | 0% | 4.1% |
| Weak Positive ~ 0.3 x LoD (0.043TCID$_{50}$/mL) | 90 | 87 | 96.7% | 90.7% | 98.9% |
| Low Positive ~ 1 x LoD (0.14TCID$_{50}$/mL) | 90 | 90 | 100% | 95.9% | 100% |
| Moderate Positive ~ 3 x LoD (0.43TCID$_{50}$/mL) | 90 | 90 | 100% | 95.9% | 100% |
| **Influenza B** | | | | | |
| Negative | 90 | 0 | 0% | 0% | 4.1% |
| Weak Positive ~ 0.3 x LoD (0.010TCID$_{50}$/mL) | 90 | 81 | 90.0% | 82.1% | 94.7% |
| Low Positive ~ 1 x LoD (0.034TCID$_{50}$/mL) | 90 | 90 | 100% | 95.9% | 100% |
| Moderate Positive ~ 3 x LoD (0.10TCID$_{50}$/mL) | 90 | 90 | 100% | 95.9% | 100% |
| **SARS-CoV-2** | | | | | |
| Negative | 90 | 0 | 0% | 0% | 4.1% |
| Weak Positive ~ 0.3 x LoD (0.035 TCID$_{50}$/mL) | 90 | 83 | 92.2% | 84.8% | 96.2% |
| Low Positive ~ 1 x LoD (0.12TCID$_{50}$/mL) | 90 | 87 | 96.7% | 90.7% | 98.9% |
| Moderate Positive ~ 3 x LoD (0.35TCID$_{50}$/mL) | 90 | 90 | 100% | 95.9% | 100% |
| **pan-Sarbecovirus** | | | | | |
| Negative | 90 | 0 | 0% | 0% | 4.1% |
| Weak Positive ~ 0.06 x LoD (0.035TCID$_{50}$/mL) | 90 | 73 | 81.1% | 71.8% | 87.9% |
| Low Positive ~ 0.2x LoD (0.12TCID$_{50}$/mL) | 90 | 87 | 96.7% | 90.7% | 98.9% |
| Moderate Positive ~ 0.6x LoD (0.35TCID$_{50}$/mL) | 90 | 90 | 100% | 95.9% | 100% |

**Table 23** Overall mean, standard deviation, and percent coefficient of variation for Ct values by positive panel member

| Target Concentration | Positivity Rate | Mean Ct | Between instrument | | Between lot | | Between day | | Between run | | Within run | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD | CV% | SD | CV% | SD | CV% | SD | CV% | SD | CV% | SD | CV% |
| **Influenza A** | | | | | | | | | | | | | | |
| Weak Positive ~ 0.3 x LoD (0.042 TCID50/mL) | 96.7% | 38.3 | 0.00 | 0.0 | 0.29 | 0.8 | 0.43 | 1.1 | 0.00 | 0.0 | 1.90 | 5.0 | 1.97 | 5.1 |
| Low Positive ~ 1 x LoD (0.14 TCID50/mL) | 100% | 35.7 | 0.00 | 0.0 | 0.00 | 0.0 | 0.19 | 0.5 | 0.15 | 0.4 | 0.90 | 2.5 | 0.93 | 2.6 |
| Moderate Positive ~ 3 x LoD (0.42 TCID50/mL) | 100% | 34.4 | 0.11 | 0.3 | 0.00 | 0.0 | 0.11 | 0.3 | 0.00 | 0.0 | 0.43 | 1.2 | 0.46 | 1.3 |
| **Influenza B** | | | | | | | | | | | | | | |
| Weak Positive ~ 0.3 x LoD (0.010 $TCID_{50}$/mL) | 90.0% | 35.6 | 0.11 | 0.3 | 0.00 | 0.0 | 0.236 | 0.6 | 0.09 | 0.3 | 0.62 | 1.7 | 0.67 | 1.9 |
| Low Positive ~ 1 x LoD (0.034 $TCID_{50}$/mL) | 100% | 34.7 | 0.00 | 0.0 | 0.00 | 0.0 | 0.19 | 0.5 | 0.21 | 0.6 | 0.51 | 1.5 | 0.58 | 1.7 |
| Moderate Positive ~ 3 x LoD (0.10 $TCID_{50}$/mL) | 100% | 33.8 | 0.07 | 0.2 | 0.00 | 0.0 | 0.17 | 0.5 | 0.00 | 0.0 | 0.82 | 2.4 | 0.84 | 2.5 |
| **SARS-CoV-2** | | | | | | | | | | | | | | |
| Weak Positive ~ 0.3 x LoD (0.035 $TCID_{50}$/mL) | 92.2% | 36.6 | 0.00 | 0.0 | 0.00 | 0.0 | 0.32 | 0.9 | 0.07 | 0.2 | 0.60 | 1.6 | 0.68 | 1.9 |
| Low Positive ~ 1 x LoD (0.12 $TCID_{50}$/mL) | 96.7% | 35.7 | 0.06 | 0.2 | 0.07 | 0.2 | 0.00 | 0.0 | 0.05 | 0.1 | 0.40 | 1.1 | 0.42 | 1.2 |
| Moderate Positive ~ 3 x LoD (0.35 $TCID_{50}$/mL) | 100% | 34.6 | 0.17 | 0.5 | 0.00 | 0.0 | 0.19 | 0.6 | 0.00 | 0.0 | 0.57 | 1.7 | 0.63 | 1.8 |
| **pan-Sarbecovirus** | | | | | | | | | | | | | | |
| Weak Positive ~ 0.06 x LoD (0.035 $TCID_{50}$/mL) | 81.1% | 35.8 | 0.00 | 0.0 | 0.00 | 0.0 | 0.16 | 0.4 | 0.11 | 0.3 | 0.63 | 1.8 | 0.66 | 1.82.0 |
| Low Positive ~ 0.2 x LoD (0.12 $TCID_{50}$/mL) | 96.7% | 34.9 | 0.00 | 0.0 | 0.04 | 0.2 | 0.00 | 0.0 | 0.00 | 0.0 | 0.52 | 1.5 | 0.52 | 1.5 |
| Moderate Positive ~ 0.6 x LoD (0.35 $TCID_{50}$/mL) | 100% | 33.9 | 0.13 | 0.4 | 0.00 | 0.0 | 0.10 | 0.3 | 0.00 | 0.0 | 0.54 | 1.6 | 0.57 | 1.7 |

## Analytical specificity ( cross-reactivity and microbial interference )

A panel of 40 viruses, bacteria, and fungi (including those commonly found in respiratory tract) plus pooled human nasal wash was tested with cobas® SARS-CoV-2 & Influenza A/B v2 to assess analytical specificity. The organisms listed in Table 24 were spiked at concentrations of 1 x $10^5$ units/mL for viruses and 1 x $10^6$ units/mL for other organisms, unless otherwise noted. Testing was performed with each potential interfering organism in the absence and presence of influenza A, influenza B, and SARS-CoV-2 target (spiked at 4, 2, 0.10 and 0.36 $TCID_{50}$/mL, respectively). None of the organisms interfered with the test performance by generating false positive results. Testing of SARS-CoV-1 generated an expected pan-Sarbecovirus positive result. Detection of influenza A, influenza B, and SARS-CoV-2 targets was not affected in the presence of the organisms tested. Potential cross-reactivity of influenza C, *Leptospira interrogans*, *Pneumocystis jirovecii*, *Chlamydia psittaci*, *Bacillus anthracis* and *Coxiella burnetii* was evaluated in silico. Based on the in silico analyses, selected organisms are highly unlikely to interfere with the performance of cobas® SARS-CoV-2 & Influenza A/B v2.

**Table 24** Microorganisms tested for analytical specificity/cross reactivity

| Microorganism | Concentration |
|---|---|
| Adenovirus (AdV-1) | 1.0E+05 $TCID_{50}$/mL |
| *Bordetella pertussis* | 1.0E+06 CFU/mL |
| *Candida albicans* | 1.0E+06 CFU/mL |
| *Chlamydia pneumoniae* | 7.9E+04 $TCID_{50}$/mL |
| *Corynebacterium diphtheriae* | 1.0E+06 CFU/mL |
| Cytomegalovirus | 1.0E+05 IU/mL |
| Enterovirus (EV68) | 1.0E+05 $TCID_{50}$/mL |
| Epstein Barr virus | 1.0E+05 cp/mL |
| *Escherichia coli* | 1.0E+06 CFU/mL |
| *Haemophilus influenzae* | 1.0E+06 CFU/mL |
| Human coronavirus 229E | 1.0E+05 $TCID_{50}$/mL |
| Human coronavirus HKU1 | 6.9E+04 genome cp/mL |
| Human coronavirus NL63 | 7.0E+03 $TCID_{50}$/mL |
| Human coronavirus OC43 | 1.0E+05 $TCID_{50}$/mL |
| Human Metapneumovirus | 1.0E+05 $TCID_{50}$/mL |
| *Lactobacillus acidophilus* | 5.0E+05 CFU/mL |
| *Legionella pneumophila* | 1.0E+06 CFU/mL |
| *Legionella longbeachae* | 1.0E+06 CFU/mL |
| Measles virus | 1.0E+05 $TCID_{50}$/mL |
| MERS coronavirus | 1.0E+05 cp/mL |
| *Moraxella catarrhalis* | 1.0E+06 CFU/mL |
| Mumps Virus | 1.0E+05 U/mL |
| *Mycobacterium bovis* | 1.0E+05 CFU/mL |
| *Mycoplasma pneumoniae* | 1.0E+06 CCU/mL |
| *Neisseria elongata* | 1.0E+06 CFU/mL |
| *Neisseria meningitidis* | 1.0E+06 CFU/mL |
| Parainfluenza virus 1 | 1.0E+05 $TCID_{50}$/mL |
| Parainfluenza virus 2 | 1.0E+05 $TCID_{50}$/mL |
| Parainfluenza virus 3 | 1.0E+05 $TCID_{50}$/mL |
| Parainfluenza virus 4 | 1.0E+05 $TCID_{50}$/mL |
| Parechovirus | 1.0E+05 U/mL |
| *Pseudomonas aeruginosa* | 1.0E+06 CFU/mL |
| Respiratory syncytial virus | 1.0E+05 PFU/mL |
| Human Rhinovirus | 1.0E+05 PFU/mL |
| SARS coronavirus (SARS-CoV-1) | 1.0E+07 PFU/mL |
| *Staphylococcus aureus* | 1.0E+06 CFU/mL |
| *Staphylococcus epidermidis* | 1.0E+06 CFU/mL |
| *Streptococcus salivarius* | 1.0E+06 CFU/mL |
| *Streptococcus pneumoniae* | 1.0E+06 CFU/mL |
| *Streptococcus pyogenes* | 1.0E+06 CFU/mL |

## Co-infection ( competitive interference )

To assess potential competitive interference between influenza A, influenza B, and SARS-CoV-2, samples were tested using cobas® SARS-CoV-2 & Influenza A/B v2 in replicates of 4 where low concentrations (0.42, 0.10 and 0.36 $TCID_{50}$/mL for influenza A, influenza B, and SARS-CoV-2, respectively) of any two targets were mixed with very high (1.0E+05 Units/mL) concentrations of the third target. None of the targets present at very high concentration interfered with the detection of low levels of the other two targets

## Collection media equivalence

Equivalence between different collection media (UTM-RT®, cobas® PCR Media, and saline) was evaluated using one strain each for influenza A (A/Kansas/14/2017 (H3N2)), influenza B (B/Phuket/3073/2013 (Yamagata lineage)) and SARS-CoV-2 (USA-WA1/2020, heat-inactivated culture). Testing was performed using cobas® SARS-CoV-2 & Influenza A/B. Virus cultures were reformulated to a target concentration of approximately 2x LoD into simulated clinical matrix formulated either in Universal Transport Media (UTM-RT®), cobas® PCR Media (CPM), or in 0.9% physiological saline. A total of 21 replicates were tested for each collection media type. All replicates tested were positive in all simulated matrices for influenza A and influenza B. For SARS-CoV-2, positivity rates were 100% for both UTM-RT® and CPM and 95.2% for saline.

# Clinical performance evaluation

First, the clinical performance was evaluated at one external site using archived nasopharyngeal swab (NPS) samples from patients with signs and symptoms of a respiratory infection, collected in UTM-RT® or UVT between 2014 and 2020 for the SARS-CoV-2 and influenza B components with cobas® SARS-CoV-2 & Influenza A/B. Clinical samples were collected by qualified personnel according to the package insert of the collection device.

This clinical evaluation study included a total of 349 NPS samples, 57 of which were longitudinal samples from COVID-19 patients. Two FDA cleared molecular tests were utilized as the comparator test for assessment of performance of the cobas® SARS-CoV-2 & Influenza A/B, one for SARS-CoV-2 and one for influenza B. One of the 349 NPS samples did not have a valid comparator SARS-CoV-2 result and five of the 349 NPS samples did not have valid comparator influenza A/B results, therefore, were excluded from the performance calculations for SARS-CoV-2 and influenza B, respectively.

In a subsequent clinical evaluation, the performance of the cobas® SARS-CoV-2 & Influenza A/B v2 was assessed for the influenza A component at one internal site using archived NPS and NS samples from patients with signs and symptoms of a respiratory infection, collected in UTM-RT® or UVT in 2022-2023. Clinical samples were collected by qualified personnel according to the package insert of the collection device. This clinical evaluation study included a total of 75 NPS and 75 nasal swab (NS) evaluable samples. An FDA cleared molecular assay was utilized as the comparator test for assessment of performance of the assay for the influenza A component.

As shown in Table 25, cobas® SARS-CoV-2 & Influenza A/B and cobas® SARS-CoV-2 & Influenza A/B v2 demonstrated high percent agreement with the comparator test for the detection of SARS-CoV-2, influenza A and influenza B.

**Table 25** Comparison of cobas® SARS-CoV-2 & Influenza A/B and cobas® SARS-CoV-2 & Influenza A/B v2 with the comparator tests.

| Virus | Number of Samples | Test Results | | | | Agreement Statistics | | |
|---|---|---|---|---|---|---|---|---|
| | | Concordant Positive (N) | Discordant Positive (N) | Concordant Negative (N) | Discordant Negative (N) | Agreement Parameter | Percent Agreement (%) | 95% CI (LCL, UCL)* |
| SARS-CoV-2[#] | 348 | 53 | 6 | 287 | 2 | PPA | 96.4% | (87.7%, 99.0%) |
| | | | | | | NPA | 98.0% | (95.6%, 99.1%) |
| Influenza A[†] | 150[a] | 50 | 0 | 100 | 0 | PPA | 100.0% | (92.9%, 100.0%) |
| | | | | | | NPA | 100.0% | (96.3%, 100.0%) |
| Influenza B | 344 | 37 | 1 | 306 | 0 | PPA | 100.0% | (90.6%, 100.0%) |
| | | | | | | NPA | 99.7% | (98.2%, 99.9%) |

PPA = Positive Percent Agreement

NPA = Negative Percent Agreement

CI = confidence interval; LCL = Lower confidence Limit; UCL = Upper confidence Limit

*Confidence interval is calculated using Wilson's Score method

[#]A positive result is defined as detection of either of the two SARS-CoV-2 or pan-Sarbecovirus target of the assay

[†]Including six H1N1pdm09 positive samples containing the C124A and G141A mutations in the M gene

[a] NPS and NS samples combined

Discordant results between the cobas® SARS-CoV-2 & Influenza A/B assay and the comparator methods were observed for 9 samples. Of these, 8 were longitudinal samples with discordant results for SARS-CoV-2 that showed late Ct values (between 35-43). The candidate test detected an additional influenza B virus positive sample compared to the comparator. Post-PCR analysis of the amplicon from the discordant samples confirmed the presence of SARS-CoV-2 but not influenza B.

cobas® SARS-CoV-2 & Influenza A/B was further evaluated in a prospective clinical study in comparison with an FDA cleared test with fresh NPS and NS clinical samples. A total of 604 NPS and a total of 608 NS samples (304 self-collected and 304 health care worker collected) with valid results by the comparator method were evaluated. The PPA for influenza B was 100% (95% Score CI of 99% to 100%) for NPS samples and 99.8% (95% Score CI of 99.1% to 100%) for NS samples. The PPA for NPS samples was not calculable for influenza B, as there were no positive samples by the comparator method. The PPA for NS samples for influenza B was 0% (0/1) with a 95% Score CI of 0% to 94.9%, as there was one positive sample by the comparator method and negative on cobas® SARS-CoV-2 & Influenza A/B.

Discordant results between the cobas® SARS-CoV-2 & Influenza A/B assay and the comparator method were observed for 2 samples. One NS sample tested positive for influenza B by the comparator method and was negative on cobas® SARS-CoV-2 & Influenza A/B. Sequencing analysis of the sample did not confirm the presence of influenza B. One NS sample tested positive for influenza B on cobas® SARS-CoV-2 & Influenza A/B and was negative on the comparator method. Post-PCR analysis of the amplicon of this discordant NS sample did not confirm the presence of influenza B.

# Additional information

## Key test features

| | |
|---|---|
| **Sample type** | Nasopharyngeal swab samples collected in the Copan UTM-RT® System or the BD™UVT System<br>Nasal swab samples collected in the Copan UTM-RT® System, the BD™UVT System, the cobas® PCR Media, and 0.9% physiological saline |
| **Minimum amount of sample required** | 0.6 mL or 1.0 mL* |
| **Sample processing volume** | 0.4 mL |
| **Test duration** | Results are available within less than 3.5 hours after loading the sample on the system. |

*Dead volume of 0.2 mL is identified for cobas® omni Secondary tubes. Dead volume of 0.6 mL is identified for the cobas® PCR Media primary tubes. Other tubes compatible with cobas® 6800/8800 Systems (consult User Assistance Guide) may have different dead volume and require more or less minimum volume.

# Symbols

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

**Table 26** Symbols used in labeling for Roche PCR diagnostics products

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

## Technical support

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

## Manufacturer and distributor

**Table 27** Manufacturer and distributor

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

Made in USA

Distributed by
Roche Diagnostics
9115 Hague Road
Indianapolis, IN 46250-0457 USA
(For Technical Assistance call the
Roche Response Center
toll-free: 1-800-526-1247)

## Trademarks and patents

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

## Copyright



IVD

## References

1. Center for Disease Control and Prevention. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institutes of Health HHS Publication No. (CDC) 21-1112, revised December 2009.
2. Clinical and Laboratory Standards Institute (CLSI). Protection of laboratory workers from occupationally acquired infections. Approved Guideline-Fourth Edition. CLSI Document M29-A4:Wayne, PA;CLSI, 2014.

# Document revision

| Document Revision Information | |
|---|---|
| Doc Rev. 1.0<br>10/2023 | First Publishing |

# cobas® SARS-CoV-2 & Influenza A/B v2

IVD

Rx Only

KIT LOT

## For USA: Emergency Use Authorization only

**USA**


**cobas**® SCoV2-FluA/B ASAP Version 12.3.0 or higher

**cobas**® 6800/8800 System Software Version 1.4 or higher

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, and influenza B, 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.

**Non-USA**


**cobas**® 5800 SCoV2-FluA/B ASAP Version 1.2.0 or higher

**cobas**® 5800 Software Version 1.0 or higher


**cobas**® SCoV2-FluA/B ASAP Version 12.3.0 or higher

**cobas**® 6800/8800 System Software Version 1.4 or higher

**USA**

website: http://e-labdoc.roche.com
Product No.: 10033401190
10033479001-01 Doc Rev. 1.0

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website: http://e-labdoc.roche.com
Method Sheet Catalog No.: 10033401190 Doc Rev 1.0

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